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Published

With international search report.

(54) Title: OXAZOLIDINONE COMBINATORIAL LIBRARIES, COMPOSITIONS AND METHODS OF PREPARATION

(57) Abstract

Oxazolidinones and methods for their synthesis are provided. Also provided are combinatorial libraries comprising oxazolidinones, and methods to prepare the libraries. Further provided are methods of making biologically active oxazolidinones as well as pharmaceutically acceptable compositions comprising the oxazolidinones. The methods of library preparation include the attachment of oxazolidinones to a solid support. The methods of compound preparation in one embodiment involve the reaction of an iminophosphorane with a carbonyl containing polymeric support.

CLAIMS

What is claimed is:

1. A method for the solid phase synthesis of oxazolidinones, comprising the steps of:

a) attaching an olefin to a solid support;

b) oxidizing the olefin to provide an epoxide functionality;

c) opening the epoxide with an amine to form an amino alcohol; and

d) cyclizing the amino alcohol using a phosgene equivalent.

2. The method according to claim 1, where the olefin is an allylic amine or allylamine.

3. The method according to claim 1, where the amine is an amino acid, or an aromatic amine.

4. A method for the synthesis of oxazolidinone combinatorial libraries, comprising the steps of:

a) attaching an olefin group to an array of solid supports;

b) oxidizing the individual olefin groups to provide an array of solid support bound epoxides; and

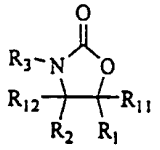
c) opening the epoxide with an amine to form an amino alcohol; and

d) cyclizing the amino alcohol using a phosgene equivalent.

5. The method according to claim 4, where the olefin is an allylic amine, or allylamine.

6. The method according to claim 4, where the amine units are amino acids or aromatic amines.

7. An oxazolidinone combinatorial library, where the oxazolidinones comprising the library are of the following structure:



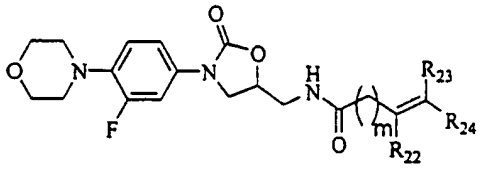
1a

where R_1 is selected from the group consisting of alkyl, heteroalkyl, aryl and heteroaryl, R_2 is selected from the group consisting of hydrogen, alkyl, heteroalkyl, aryl and heteroaryl, R_3 is selected from the group consisting of hydrogen, alkyl, heteroalkyl, aryl and heteroaryl, R_{11} is selected from the group consisting of hydrogen, alkyl, heteroalkyl, aryl and heteroaryl, and R_{12} is selected from the group consisting of hydrogen, alkyl, heteroalkyl, aryl and heteroaryl.

8. The combinatorial library according to claim 7, where R_3 is selected from the group consisting of aryl and heteroaryl, and further where the aryl and heteroaryl groups are the aryl and heteroaryl groups attached to the amines of Table 2 and Figures 29, 30, and 31.

9. The combinatorial library according to claim 7, where R_3 is a heteroaryl group selected from the group consisting of a pyridyl group, a thienylphenyl group, an oxazolyl group, a pyrrolyl group, and a morpholinofluorophenyl group.

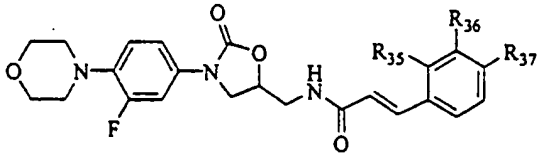
10. An antimicrobial compound where the compound is of the structure:



where m is 0, 1, 2 or 3, and where R_{22}, R_{23} and R_{24} are independently selected from the group consisting of hydrogen, alkyl, heteroalkyl, aryl and heteroaryl.

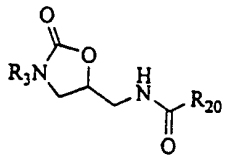
11. The antimicrobial compound according to claim 10, where m is 0, and where R_{22} and R_{23} are hydrogen, and where R_{24} is an aryl group.

12. The antimicrobial compound according to claim 11, where the compound is of the structure:

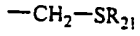


where R_{35}, R_{36} and R_{37} are independently selected from the group consisting of hydrogen, electron withdrawing group, alkyl, heteroalkyl, aryl and heteroaryl.

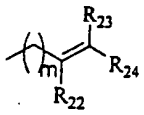
13. An antimicrobial compound, where the compound has the following structure:



where R_3 is selected from the group consisting of aryl and heteroaryl, and where R_{20} is selected from the group consisting of structures A, B, C, I, J and K

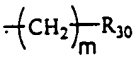


A

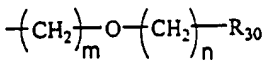


B

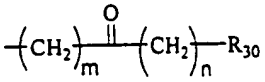
C



I



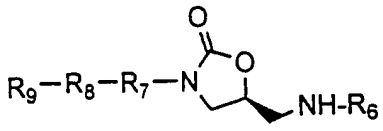
J



K

wherein m is 0, 1, 2 or 3, and where n is 0, 1, 2 or 3, and wherein R_{21} is selected from the group consisting of alkyl, heteroalkyl, aryl and heteroaryl, and where R_{22}, R_{23} and R_{24} are independently selected from the group consisting of hydrogen, alkyl, heteroalkyl, aryl and heteroaryl, and where R_{25} is selected from the group consisting of hydrogen, alkyl, heteroalkyl, aryl and heteroaryl, and where R_{30} is selected from the group consisting of alkyl, heteroalkyl, aryl and heteroaryl.

14. A compound of formula 2c:



2c

wherein:

R_6 is acyl or sulfonyl;

R_7 is aryl or heteroaryl;

R_8 is C_1-C_7 alkyl, NR, O, S, C(=O)NR, NRC(=O), C(=O), C(=O)O, OC(=O), S(=O), SO_2, SO_2NR, $NRSO_2$, NRCONR', or $(CH_2)_nO$, wherein n = 0-6, and wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl; and

R_9 is hydrogen, OH, alkyl, aryl, heteroalkyl, or heteroaryl.

15. The compound of claim 14 wherein:

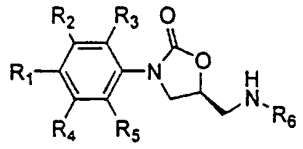
R_6 is C(=O)R, wherein R is H, alkyl, or aryl;

R_7 is aryl;

R_8 is NH(C=O) or NR'(C=O), where R' is H, alkyl, or aryl; and

R_9 is hydrogen, pyridinyl, thiazolyl, benzothiazolyl, isothiazolyl, quinolinyl, 1,3,4-triazolyl, or 1,3,4-thiadiazolyl.

16. A compound of the structure **1b**:



1b

wherein R_2, R_3, R_4 and R_5 are, independently, hydrogen alkyl, heteroalkyl, heteroaryl or an electron withdrawing group; R_6 is acyl or sulfonyl; and, R_1 is one of the following functional groups: $C(O)NR_7R_8$, wherein R_7 and R_8 are, independently, hydrogen, alkyl, heteroalkyl, aryl or heteroaryl; $C(O)OR_9$, wherein R_9 is hydrogen, alkyl, heteroalkyl, aryl or heteroaryl; $C(O)R_{10}$, wherein R_{10} is hydrogen, alkyl, heteroalkyl, aryl or heteroaryl; SR_{11}, wherein R_{11} is hydrogen, alkyl, heteroalkyl, aryl or heteroaryl; $S(O)_2R_{11}$, wherein R_{11} is hydrogen, alkyl, heteroalkyl, aryl or heteroaryl; $S(O)R_{11}$, wherein R_{11} is hydrogen, alkyl, heteroalkyl, aryl or heteroaryl; $NR_{12}R_{13}$, wherein R_{12} and R_{13} are, independently, hydrogen, acyl, sulfonyl, alkyl, heteroalkyl, aryl or heteroaryl; 2-oxazolyl, wherein R_{14} is at the 4-position and R_{15} is at the 5-position of the oxazolyl, and wherein R_{14}

and R_{15} are, independently, hydrogen, alkyl, heteroalkyl, aryl, heteroaryl or an electron withdrawing group; 2-aminothiazolyl, wherein R_{16} is at the 4-position and R_{17} is at the 5-position of the thiazole, and wherein R_{16} and R_{17}, are, independently, hydrogen, alkyl, heteroalkyl, aryl, heteroaryl or an electron withdrawing group; and, $CH_2NR_{18}R_{19}$, wherein R_{18} and R_{19} are, independently, hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, acyl or sulfonyl.

17. A combinatorial library of compounds according to claim 16.

18. A compound of claim 16, wherein R_1 is $C(O)NR_7R_8$, $C(O)OR_9$, $C(O)R_{10}$, SR_{11}, $S(O)_2R_{11}$, $S(O)R_{11}$ or $NR_{12}R_{13}$.

19. A compound according to claim 16, wherein R_1 is $C(O)NR_7R_8$.

20. A compound according to claim 16, wherein R_1 is $C(O)OR_9$.

21. A compound according to claim 16, wherein R_1 is $C(O)R_{10}$.

22. A compound according to claim 16, wherein R_1 is SR_{11}.

23. A compound according to claim 16, wherein R_1 is $NR_x(C=O)R_y$, wherein R_x and R_y are independently hydrogen, alkyl, heteroalkyl, aryl, or heteroaryl.

24. A compound according to claim 16, wherein R_1 is $NR_x(SO_2)R_y$, wherein R_x and R_y are independently hydrogen, alkyl, heteroalkyl, aryl, or heteroaryl with the proviso that R_y is not H.

25. A compound according to claim 16, wherein R_1 is $NR_{12}R_{13}$.

26. A compound according to claim 16, wherein R_1 is 2-oxazolyl, wherein R_{14} is at the 4-position and R_{15} is at the 5-position of the oxazole group.

27. A compound according to claim 16, wherein R_1 is 2-aminothiazolyl, wherein R_{16} is at the 4-position and R_{17} is at the 5-position of the aminothiazolyl group.

28. A compound according to claim 16, wherein R_1 is $CH_2NR_{18}R_{19}$.

29. A compound according to claim 18, wherein R_3, R_4 and R_5 are hydrogen.

30. A compound according to claim 29, wherein R_2 is fluorine.

31. A compound according to claim 30, wherein, R_6 is $C(O)CH_3$.

32. A compound according to claim 31, wherein R_1 is $C(O)NR_7R_8$ and R_7 is hydrogen.

33. A compound according to claim 32, wherein R_8 is heteroaryl.

34. A biologically active oxazolidinone derived from a combinatorial library

according to claim 17.

35. A compound according to claim 19, wherein R_3, R_4 and R_5 are hydrogen.

36. A compound according to claim 26, wherein R_3, R_4 and R_5 are hydrogen.

37. A compound according to claim 27, wherein R_3, R_4 and R_5 are hydrogen.

38. A compound according to claim 35, wherein R_2 is fluorine.

39. A compound according to claim 36, wherein R_2 is fluorine.

40. A compound according to claim 37, wherein R_2 is fluorine.

41. A compound according to claim 38, wherein R_6 is $C(O)CH_3$, and NR_7R_8 is NH(5'-(5-aminopyridine-2-yl)thiopyridine-3'-yl) or NH(pyridine-3-yl).

42. A compound according to claim 38, wherein R_6 is $C(O)CH_2SMe$, and NR_7R_8 is NH(5-chloropyridine-3-yl).

43. A compound according to claim 38, wherein R_6 is C(O)CHCH(pyridine-3-yl), and R_7R_8 is NH(5-chloropyridine-3-yl).

44. A method of preparing the combinatorial libraries according to claim 17, comprising the steps of:

a) attaching a plurality of aryl oxazolidinones to a plurality of solid supports;

b) functionalizing the 4-position of the aryl groups of the attached oxazolidinones; and, optionally,

c) removing the oxazolidinones from the solid supports.

45. The method according to claim 44, wherein the aryl oxazolidinone is attached to a solid support through the reaction of an iminophosphorane with a carbonyl containing resin to form an imine.

46. The method according to claim 44, wherein the aryl oxazolidinone is attached to a solid support through the reaction of an amine with a carbonyl containing resin to form an imine.

47. The method according to claim 45, wherein the attachment further comprises the step of reducing the imine.

48. The method according to claim 46, wherein the attachment further comprises the step of reducing the imine.

49. A method of synthesizing the compounds according to claim 16, wherein

the method comprises the steps of:

a) providing an iminophosphorane;

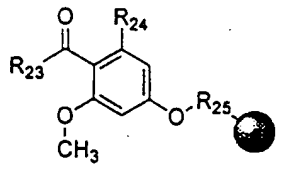
b) mixing the iminophosphorane with a resin that comprises carbonyl groups to form an imine intermediate; and,

c) reducing the imine intermediate to afford a compound attached to the resin through an amine linkage.

50. A method according to claim 49, wherein the iminophosphorane is provided from an azide that is reacted with a phosphine.

51. A method according to claim 49, wherein the iminophosphorane is provided from an amine that is reacted with a (trisubstituted)phosphine dihalide.

52. A method according to claim 49, wherein the resin comprising carbonyl groups is of the structure



1c

wherein R_{23} is hydrogen, alkyl, aryl, O-alkyl or O-aryl; R_{24} is hydrogen, CH_3O or NO_2; R_{25} is $(CH_2)_nCONH$, wherein n is an integer between 1 and about 5; and, the filled circle is a polymeric support.

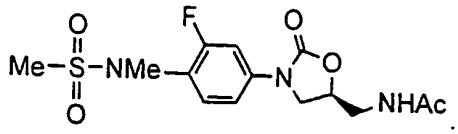
53. A method according to claim 52, wherein R_{23} is hydrogen, R_{24} is CH_3O, R_{25} is $(CH_2)_3CONH$, and the filled circle is Tentagel, (cross-linked)polystyrene, (cross-linked)polyethyleneglycol or polyethyleneglycol-polystyrene compositions.

54. A method of synthesizing a compound according to claim 16, wherein the method comprises the steps of:

a) reacting an amine with a resin that comprises carbonyl groups to form an imine intermediate; and

b) reducing the imine intermediate to afford a compound attached to the resin through an amine linkage.

55. The compound of claim 14 selected from the group consisting of



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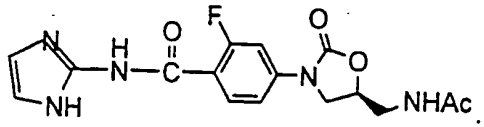

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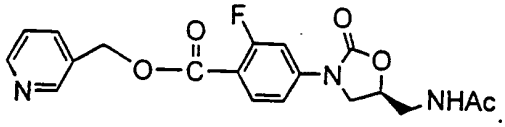

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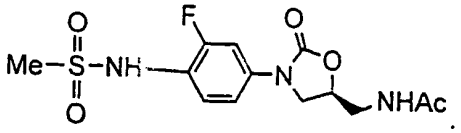
56. The compound of claim 14 selected from the group consisting of



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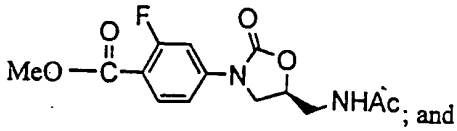

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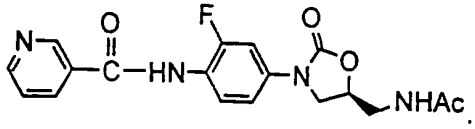
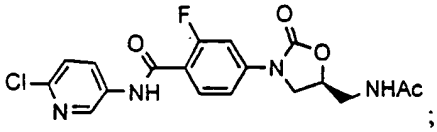


57. The compound of claim 14 selected from the group consisting of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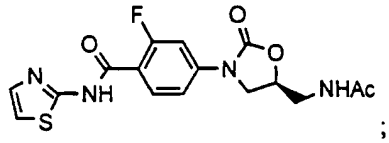
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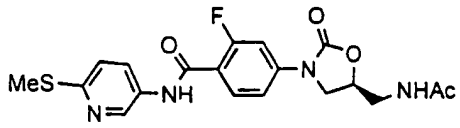

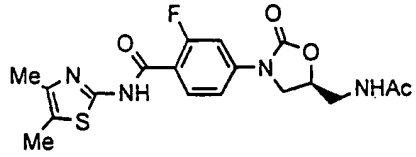
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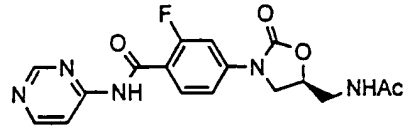
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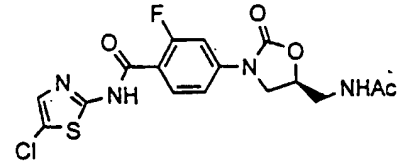
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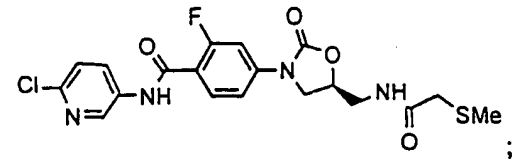
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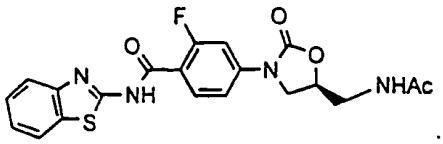
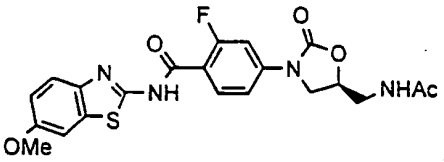
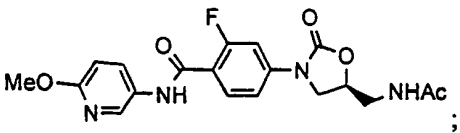


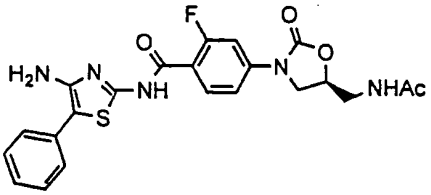
; and



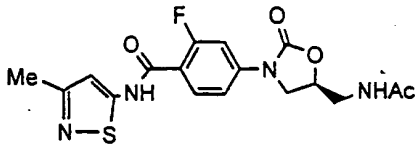
58. The compound of claim 14 selected from the group consisting of



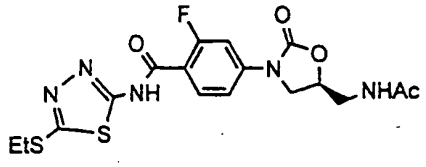
;



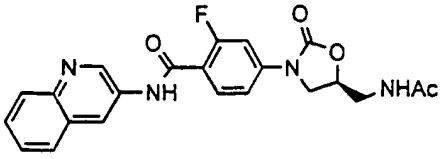
;



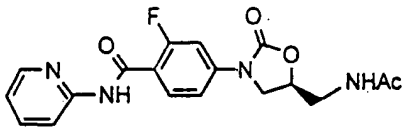
;



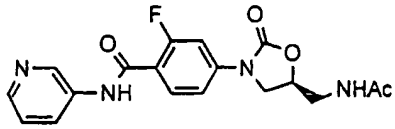
;



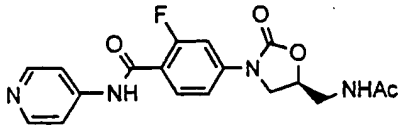
;



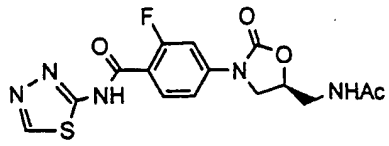
;



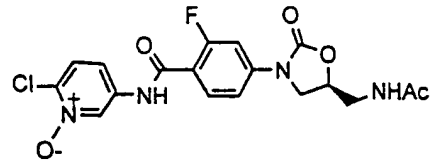
; and



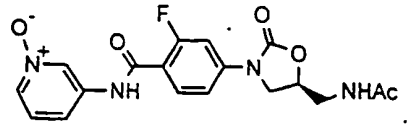
59. The compound of claim 14 selected from the group consisting of

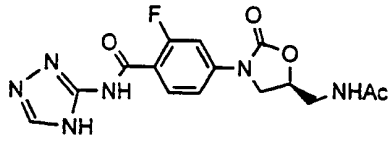


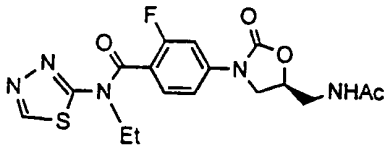
;



;


;


; and



60. The compound of claim 14 wherein:

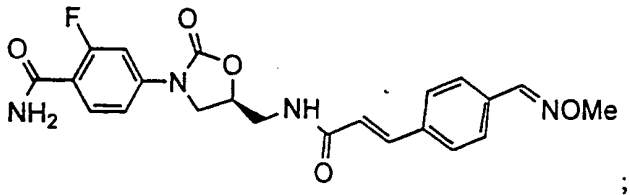
R_6 is C(=O)R, wherein R is H, alkyl, heteroalkyl, aryl or heteroaryl;

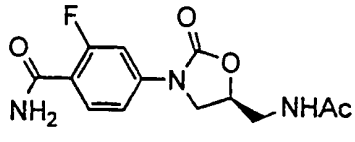
R_7 is aryl;

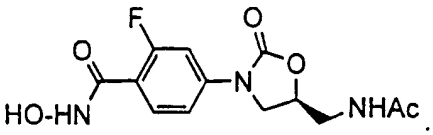
R_8 is NH(C=O); and

R_9 is hydrogen or OH.

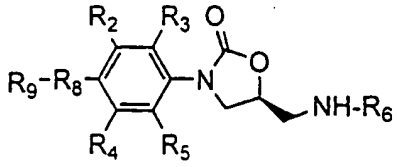
61. The compound of claim 14 wherein the compound is selected from the group consisting of:


;


; and



62. A compound of formula **3c**



3c

wherein:

R_2, R_3, R_4 and R_5 are, independently, hydrogen, alkyl, heteroalkyl, heteroaryl or an electron withdrawing group;

R_6 is acyl or sulfonyl;

R_8 is C_1-C_7 alkyl, NR, O, S, C(=O)NR, NRC(=O), C(=O), C(=O)O, OC(=O), S(=O), SO_2, SO_2NR, $NRSO_2$, NRCONR', or $(CH_2)_nO$, wherein n = 0-6, and wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl; and

R_9 is alkyl, aryl, heteroalkyl, or heteroaryl.

63. The compound of claim 62, wherein

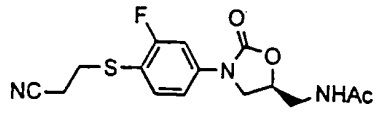
R_6 is $C(=O)CH_3$;

R_7 is aryl;

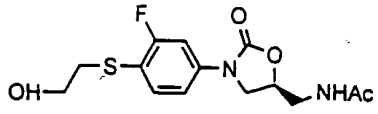
R_8 is S; and

R_9 is heteroalkyl.

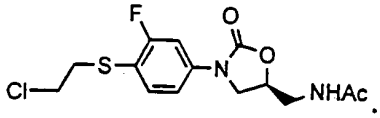
64. The compound of claim 62, wherein the compound is selected from the group consisting of



;

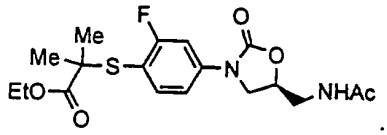


; and

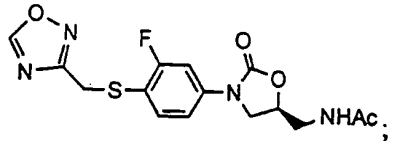


.

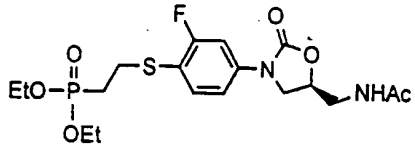
65. The compound of claim 62, wherein the compound is selected from the group consisting of



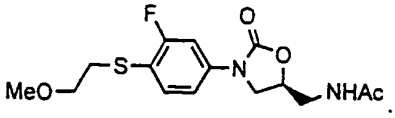
;



;

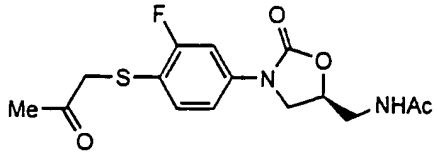


; and

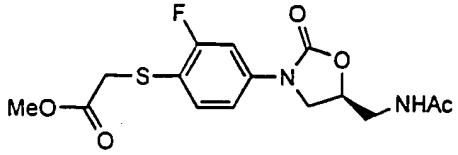


.

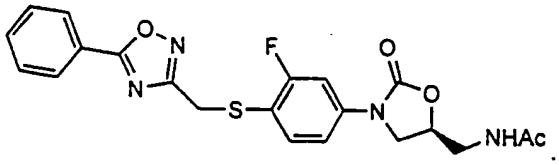
66. The compound of claim 62, wherein the compound is selected from the group consisting of



;



; and



67. The compound of claim 62 wherein:

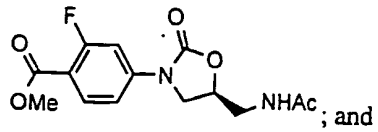
R_6 is $C(=O)CH_3$;

R_7 is aryl;

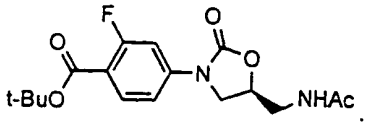
R_8 is $OC(=O)$; and

R_9 is alkyl.

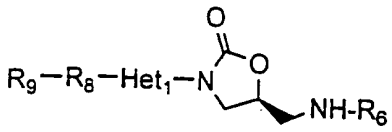
68. The compound of claim 62 selected from the group consisting of:



; and



69. A compound of formula **4c**:



4c

wherein:

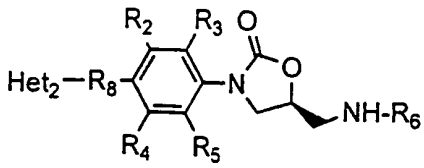
R_6 is acyl or sulfonyl;

Het_1 is heteroaryl;

R_8 is C_1-C_7 alkyl, NR, O, S, C(=O)NR, C(=O)NOR, NRC(=O), C(=O), C(=O)O, OC(=O), S(=O), SO_2, SO_2NR, $NRSO_2$, NRCONR', or $(CH_2)_nO$, wherein n = 0-6, and wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl; and

R_9 is alkyl, aryl, heteroalkyl, or heteroaryl.

70. A compound of formula **5c**:



wherein:

R_2, R_3, R_4 and R_5 are, independently, hydrogen, alkyl, heteroalkyl, heteroaryl or an electron withdrawing group;

R_6 is acyl or sulfonyl;

R_8 is C_1-C_7 alkyl, NR, O, S, C(=O)NR, NRC(=O), C(=O)NOR C(=O), C(=O)O, OC(=O), S(=O), SO_2, SO_2NR, $NRSO_2$, NRCONR', or $(CH_2)_nO$, wherein n = 0-6, and wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl; and

Het_2 is a heterocyclic group.

71. The compound of claim 70, wherein

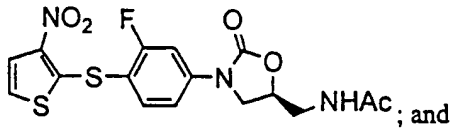
R_6 is $C(=O)CH_3$;

R_7 is aryl;

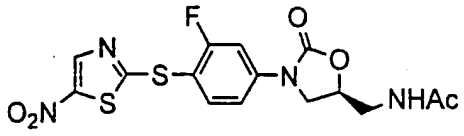
R_8 is S; and

Het_2 is a thienylphenyl or thiazolyl group.

72. The compound of claim 70 selected from the group consisting of:



; and



73. The compound of claim 70 wherein:

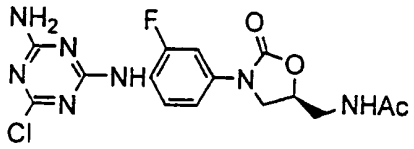
R_6 is $C(=O)CH_3$;

R_7 is aryl;

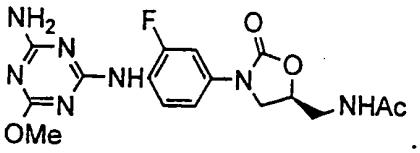
R_8 is NH; and

Het_2 is 1,3,5-triazinyl.

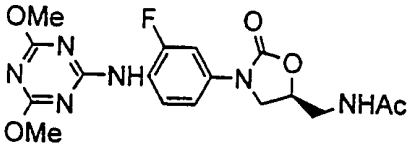
74. The compound of claim 70 selected from the group consisting of



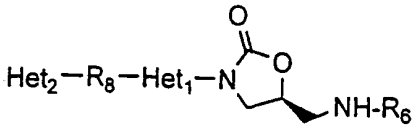
;



; and



75. A compound of formula 6c:



6c

wherein:

R_6 is acyl or sulfonyl;

R_8 is C_1-C_7 alkyl, NR, O, S, C(=O)NR, NRC(=O), C(=O)NOR C(=O), C(=O)O, OC(=O), S(=O), SO_2, SO_2NR, $NRSO_2$, NRCONR', or $(CH_2)_nO$, wherein n = 0-6, and wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl;

Het_1 is heteroaryl; and

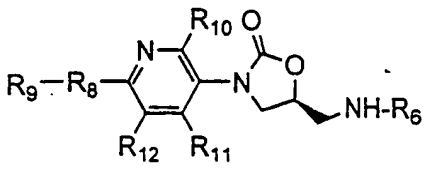
Het_2 is a heterocyclic group.

76. The compound of claim 75 wherein

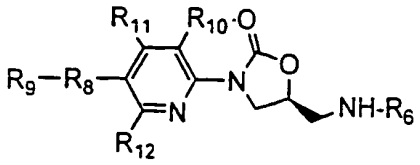
Het_1 is selected from the group consisting of thienylphenyl, thiazolyl, 1,3,4-thiadiazolyl, pyridinyl, pyrimidinyl, phenyl and fluorophenyl; and

Het_2 is selected from the group consisting of oxazolyl, isoxazolyl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3-oxadiazolyl, thienylphenyl, thiazolyl, isothiazolyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, pyrrolyl, imidazolyl, pyrazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,3-triazinyl, 1,2,4-triazinyl, tetrazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, 1,2,4-triazinyl, 1,3,5-triazinyl, and 1,2,4,5-tetrazinyl.

77. A compound of formulas 7c or 8c:



7c



8c

wherein:

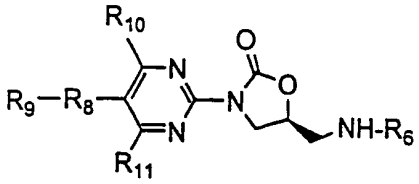
R_6 is acyl or sulfonyl;

R_8 is C_1-C_7 alkyl, NR, O, S, C(=O)NR, C(=O)NOR, NRC(=O), C(=O), C(=O)O, OC(=O), S(=O), SO_2, SO_2NR, $NRSO_2$, NRCONR', or $(CH_2)_nO$, wherein n = 0-6, and wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl;

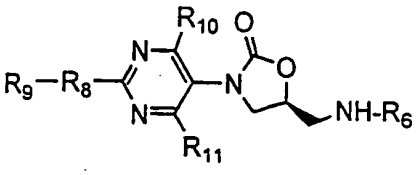
R_9 is alkyl, aryl, heteroalkyl, or heteroaryl; and

R_{10}, R_{11} and R_{12} are independently hydrogen, alkyl, aryl, heteroalkyl, electron withdrawing group, F, Cl, CN, NO_2, NR''R''', OR'', SR'', S(=O)R'', SO_2R'', C(=O)R'', C(=O)OR'', OC(=O)R'', C(=O)NR''R''', N(R'')C(=O)R''', or N-oxide group in the pyridine nuclei, wherein R'' and R''' are independently H, alkyl, heteroalkyl, aryl or heteroaryl.

78. A compound of formula **9c** or **10c**:



9c



10c

wherein:

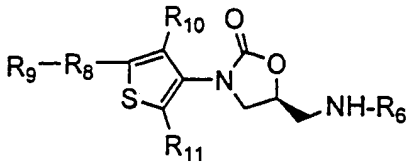
R_6 is acyl or sulfonyl;

R_8 is C_1-C_7 alkyl, NR, O, S, C(=O)NR, C(=O)NOR, NRC(=O), C(=O), C(=O)O, OC(=O), S(=O), SO_2, SO_2NR, $NRSO_2$, NRCONR', or $(CH_2)_nO$, where n = 0-6, and where R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl;

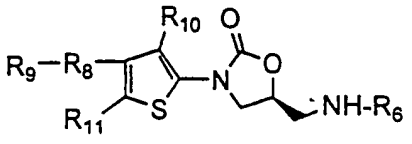
R_9 is alkyl, aryl, heteroalkyl, or heteroaryl; and

R_{10} and R_{11} are independently hydrogen, alkyl, aryl, heteroalkyl, electron withdrawing group, F, Cl, CN, NO_2, NR''R''', OR'', SR'', S(=O)R'', SO_2R'', C(=O)R'', C(=O)OR'', OC(=O)R'', C(=O)NR''R''', N(R'')C(=O)R''', or N-oxide group in the pyrimidine nuclei, wherein R' and R''' are independently H, alkyl, heteroalkyl, aryl or heteroaryl.

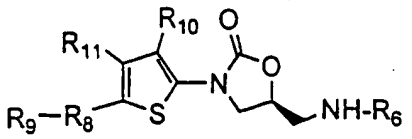
79. A compound of formula **11c**, **12c** or **13c**:



11c



12c



13c

wherein:

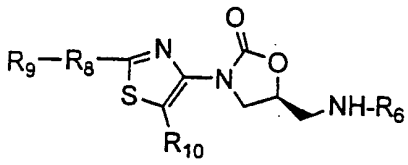
R_6 is acyl or sulfonyl;

R_8 is C_1-C_7 alkyl, NR, O, S, C(=O)NR, C(=O)NOR, NRC(=O), C(=O), C(=O)O, OC(=O), S(=O), SO_2, SO_2NR, NRSO_2, NRCONR', or $(CH_2)_n$O, wherein n = 0-6, and wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl;

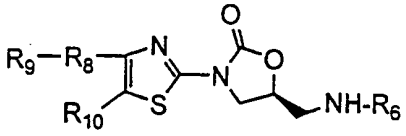
R_9 is alkyl, aryl, heteroalkyl, or heteroaryl; and

R_{10} and R_{11} are independently hydrogen, alkyl, aryl, heteroalkyl, electron withdrawing group, F, Cl, CN, NO_2, NR''R''', OR'', SR'', S(=O)R'', SO_2R'', C(=O)R'', C(=O)OR'', OC(=O)R'', C(=O)NR''R''', or N(R'')C(=O)R''', wherein R'' and R''' are independently H, alkyl, heteroalkyl, aryl or heteroaryl.

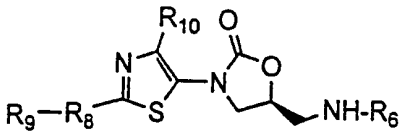
80. A compound of formula **14c, 15c** or **16c**:



14c



15c



16c

wherein:

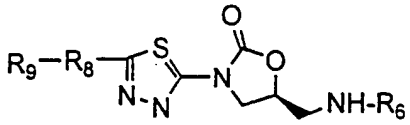
R_6 is acyl or sulfonyl;

R_8 is C_1-C_7 alkyl, NR, O, S, C(=O)NR, C(=O)NOR, NRC(=O), C(=O), C(=O)O, OC(=O), S(=O), SO_2, SO_2NR, $NRSO_2$, NRCONR', or $(CH_2)_nO$, wherein n = 0-6), and wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl;

R_9 is alkyl, aryl, heteroalkyl, or heteroaryl; and

R_{10} is hydrogen, alkyl, aryl, heteroalkyl, electron withdrawing group, F, Cl, CN, NO_2, NR''R''', OR'', SR'', S(=O)R'', SO_2R'', C(=O)R'', C(=O)OR'', OC(=O)R'', C(=O)NR''R''', or N(R'')C(=O)R''', where R'' and R''' are independently H, alkyl, heteroalkyl, aryl or heteroaryl.

81. A compound of formula **17c**:



17c

wherein:

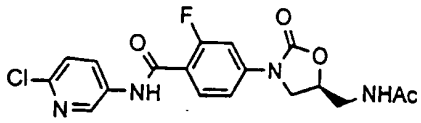
R_6 is acyl or sulfonyl;

R_8 is C_1-C_7 alkyl, NR, O, S, C(=O)NR, C(=O)NOR, NRC(=O), C(=O), C(=O)O, OC(=O), S(=O), SO_2, SO_2NR, $NRSO_2$, NRCONR', or $(CH_2)_nO$, where n = 0-6, and where R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl; and

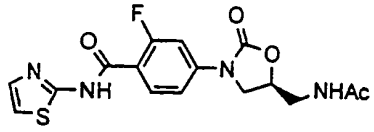
R_9 is alkyl, aryl, heteroalkyl, or heteroaryl..

82. A composition for the treatment or prevention of an infectious disorder comprising an effective amount of a compound of claim 14 and a pharmaceutically acceptable carrier.

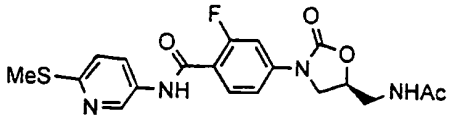
83. The composition of claim 82 wherein the compound is



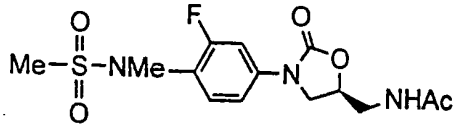
84. The composition of claim 82 wherein the compound is



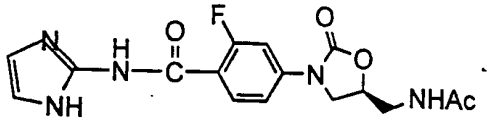
85. The composition of claim 82 wherein the compound is



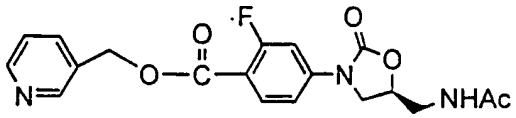
86. The composition of claim 82 wherein the compound is



87. The composition of claim 82 wherein the compound is



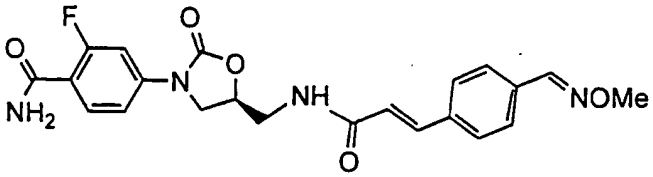
88. The composition of claim 82 wherein the compound is



89. A composition for the treatment or prevention of an infectious disorder comprising an effective amount of a compound of claim 55 and a pharmaceutically acceptable carrier.

90. A composition for the treatment or prevention of an infectious disorder comprising an effective amount of a compound of claim 57 and a pharmaceutically acceptable carrier.

91. The composition of claim 82, wherein the compound is



92. A composition for the treatment or prevention of an infectious disorder comprising an effective amount of a compound of claim 61 and a pharmaceutically acceptable carrier.

93. A composition for the treatment or prevention of an infectious disorder comprising an effective amount of a compound of claim 64 and a pharmaceutically acceptable carrier.

94. A composition for the treatment or prevention of an infectious disorder comprising an effective amount of a compound of claim 72 and a pharmaceutically acceptable carrier.

95. A method of treating or preventing an infectious disorder in a human or other animal subject, comprising administering to the subject an effective amount of a compound of claim 14.

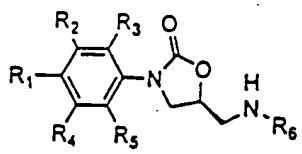
96. A method of treating or preventing an infectious disorder in a human or other animal subject, comprising administering to the subject an effective amount of a compound of claim 55.

97. A method of treating or preventing an infectious disorder in a human or other animal subject, comprising administering to the subject an effective amount of a compound of claim 57.

98. A method of treating or preventing an infectious disorder in a human or other animal subject, comprising administering to the subject an effective amount of a compound of claim 61.

99. A method of treating or preventing an infectious disorder in a human or other animal subject, comprising administering to the subject an effective amount of a compound of claim 64.

100. A method of treating or preventing an infectious disorder in a human or other animal subject, comprising administering to the subject an effective amount of a compound of claim 72.



1b

FIGURE 1

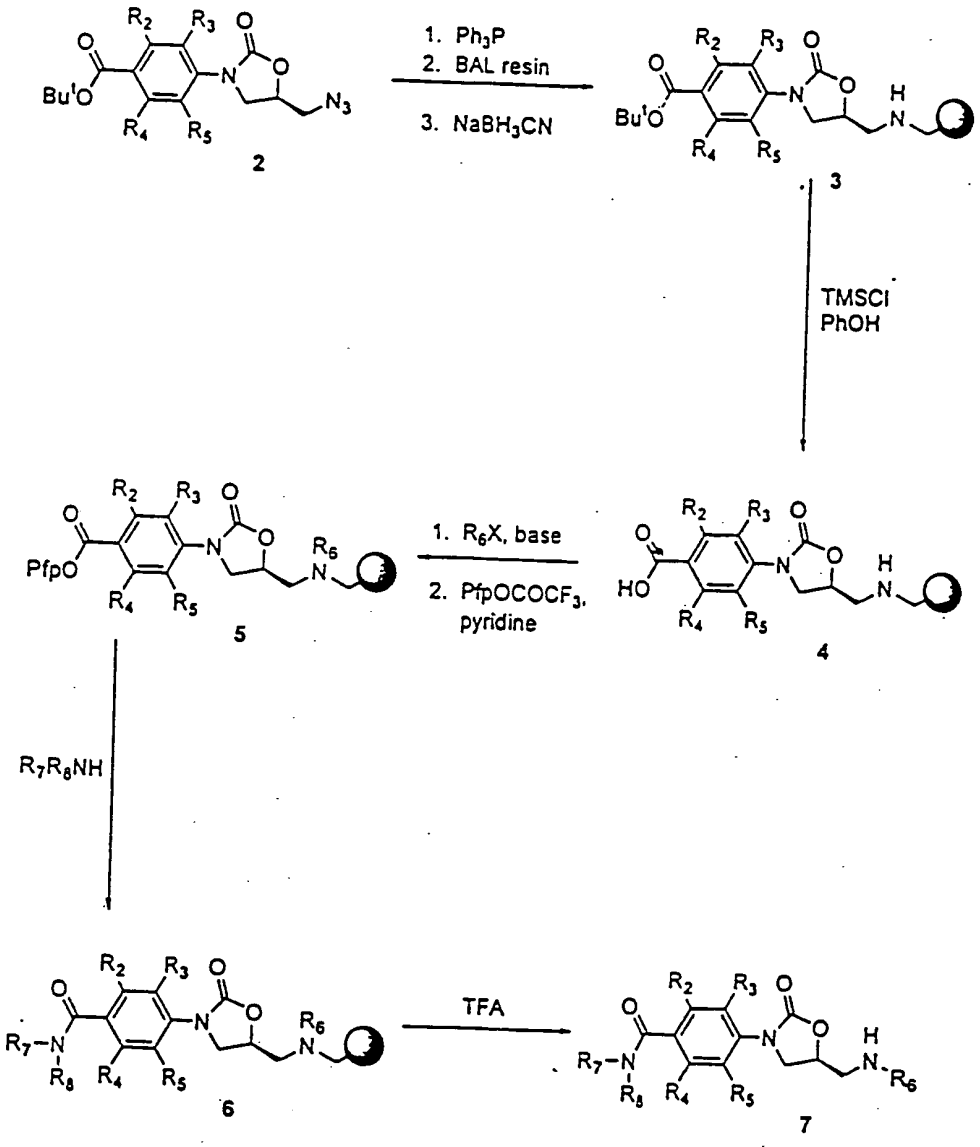

1. Ph_3P
2. BAL resin
3. $NaBH_3CN$
TMSCl
PhOH
1. R_6X, base
2. $PfpOCOCF_3$, pyridine
R_7R_8NH
TFA

FIGURE 2

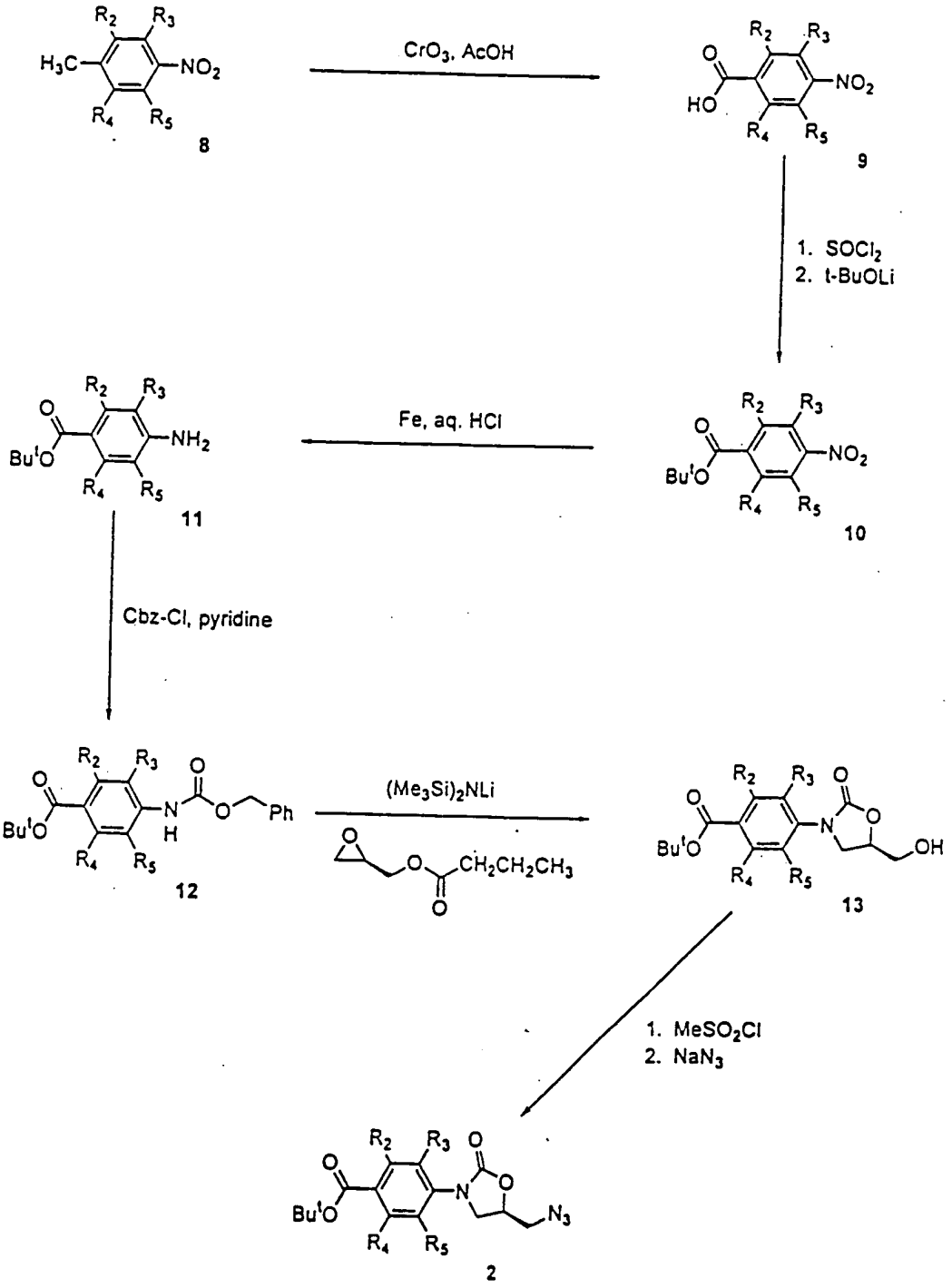

CrO_3, AcOH
1. $SOCl_2$
2. t-BuOLi
Fe, aq. HCl
Cbz-Cl, pyridine
$(Me_3Si)_2NLi$
1. $MeSO_2Cl$
2. NaN_3

FIGURE 3

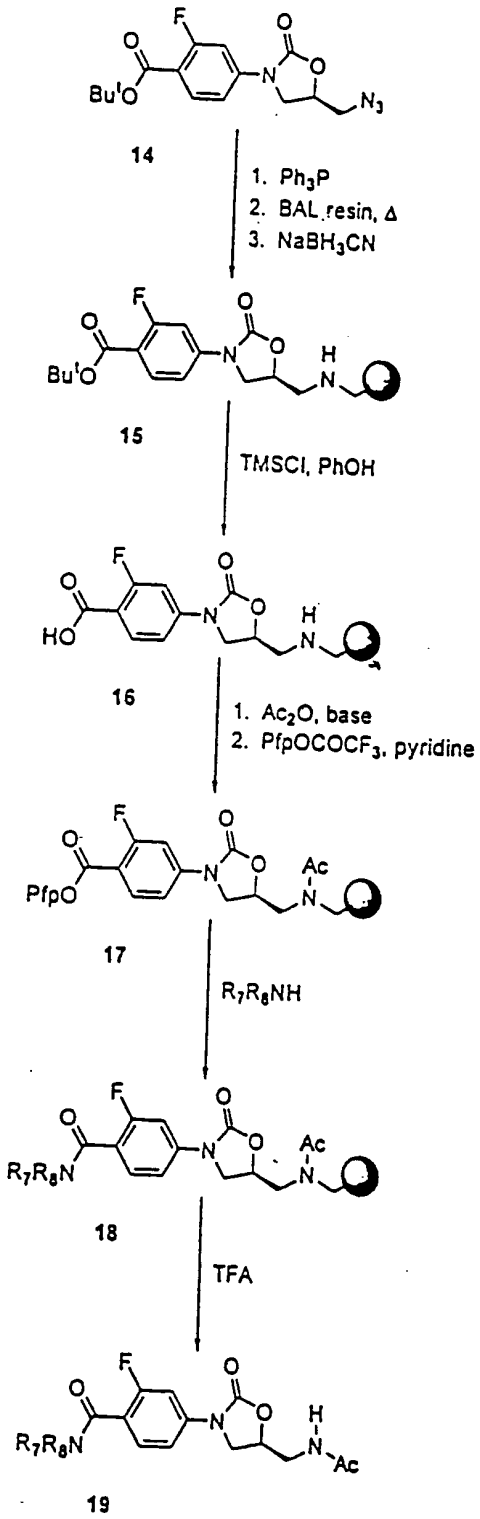

14
1. Ph_3P
2. BAL resin, Δ
3. $NaBH_3CN$
15
TMSCl, PhOH
16
1. Ac_2O, base
2. $PfpOCOCF_3$, pyridine
17
R_7R_8NH
18
TFA
19

FIGURE 4

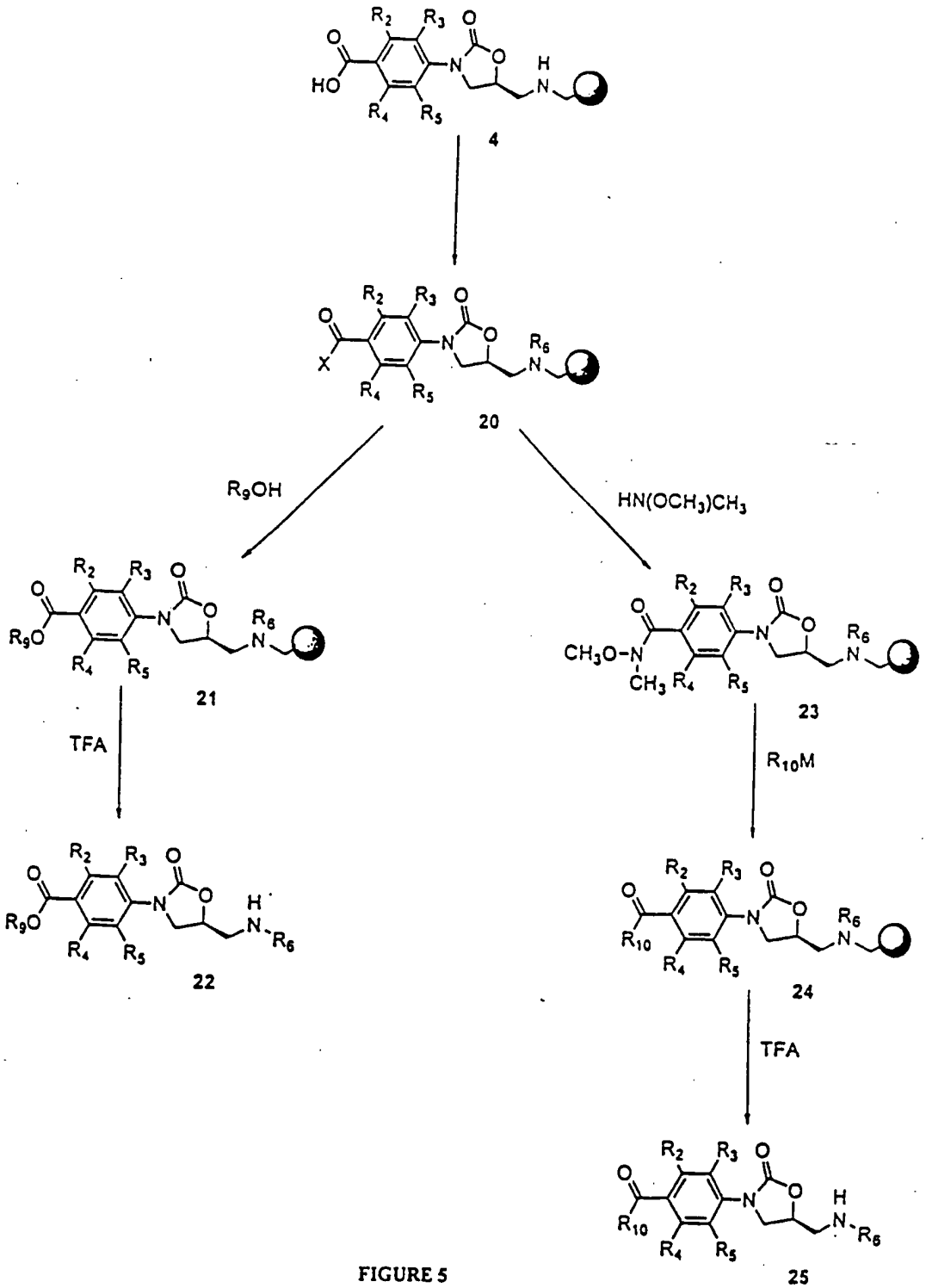


FIGURE 5

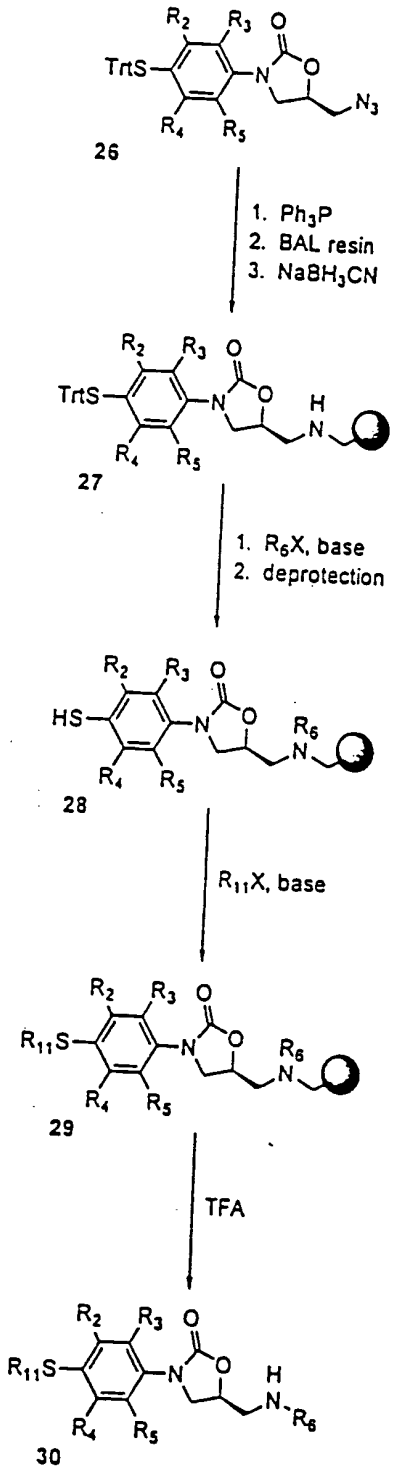

TrtS
R_2 R_3 O
N O
N_3
R_4 R_5
26
1. Ph_3P
2. BAL resin
3. $NaBH_3CN$
H N
27
1. R_6X, base
2. deprotection
HS
R_6
28
$R_{11}X$, base
$R_{11}S$
29
TFA
30

FIGURE 6

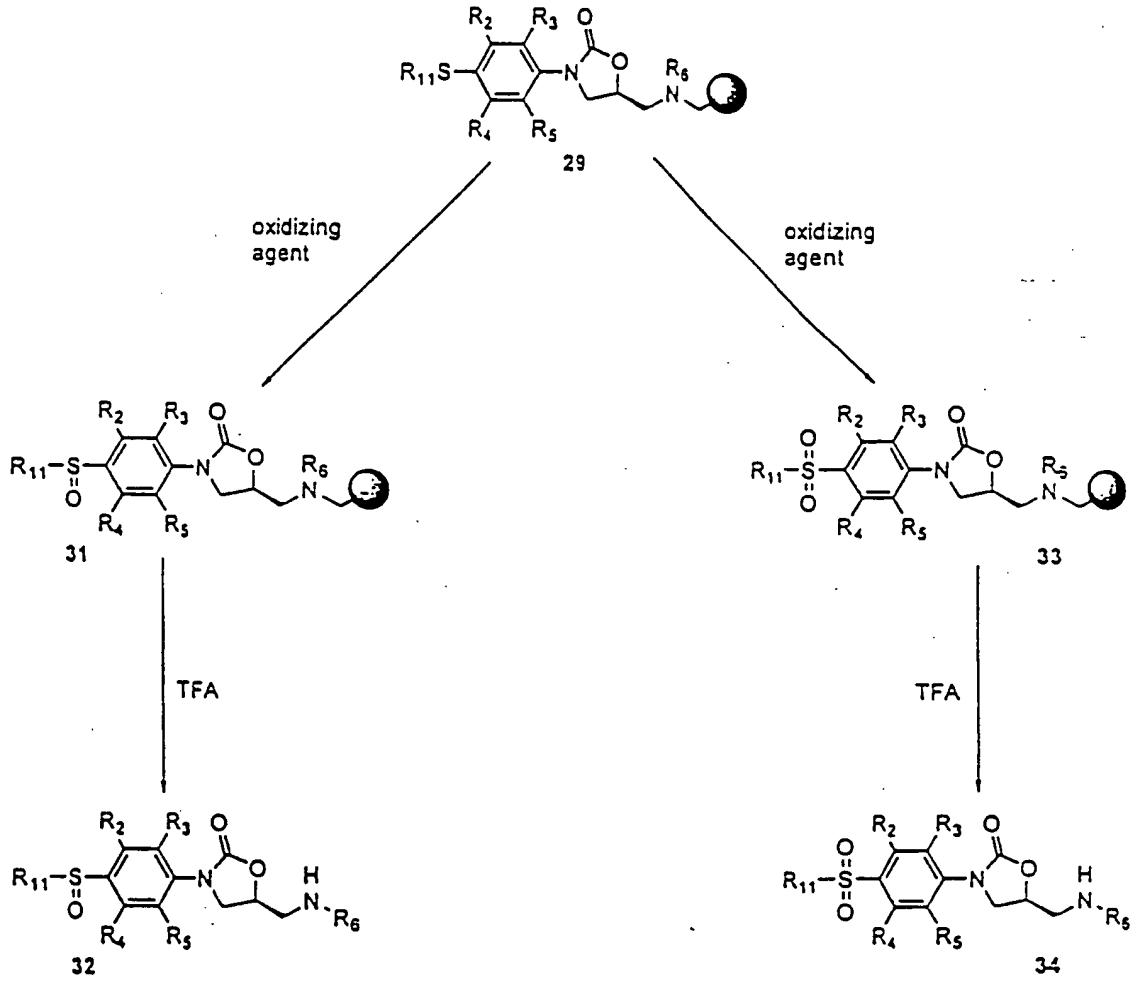


FIGURE 7

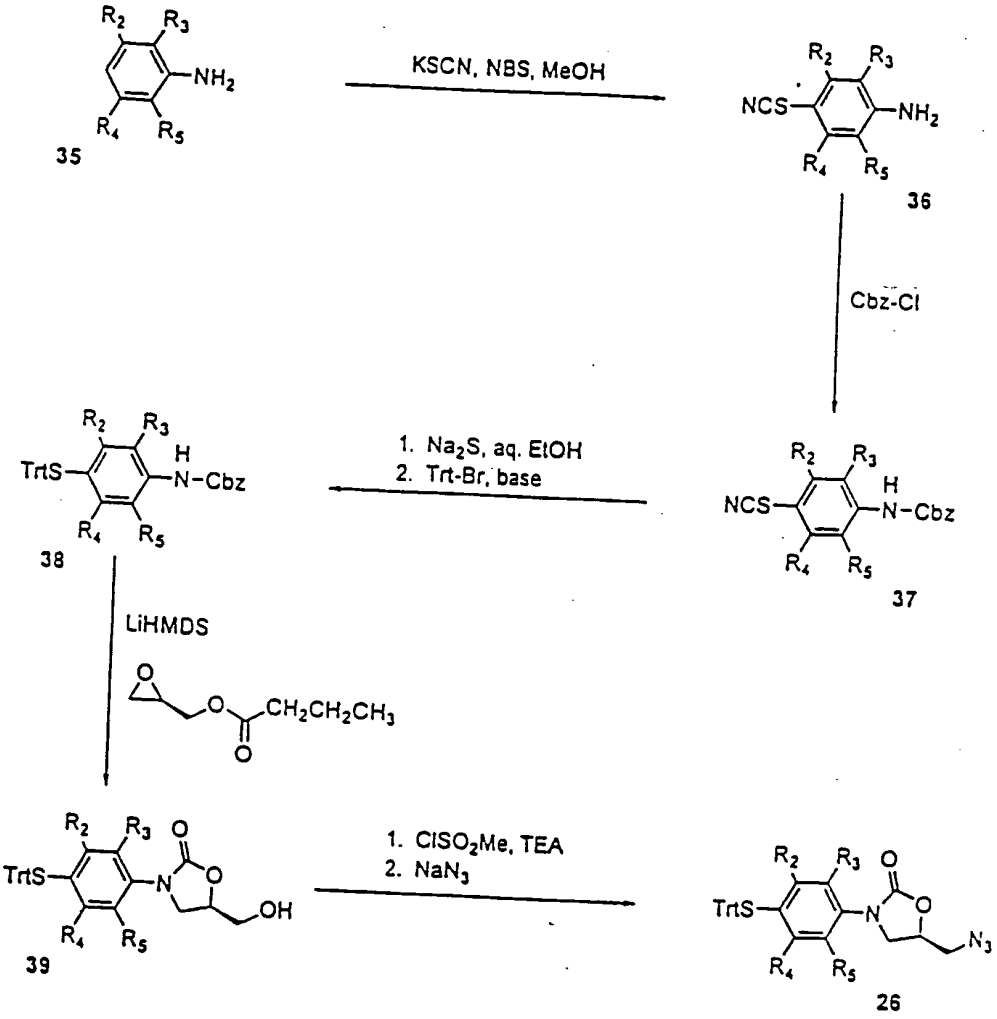

KSCN, NBS, MeOH
Cbz-Cl
1. Na_2S, aq. EtOH
2. Trt-Br, base
LiHMDS
1. $ClSO_2Me$, TEA
2. NaN_3
35
36
37
38
39
26

FIGURE 8

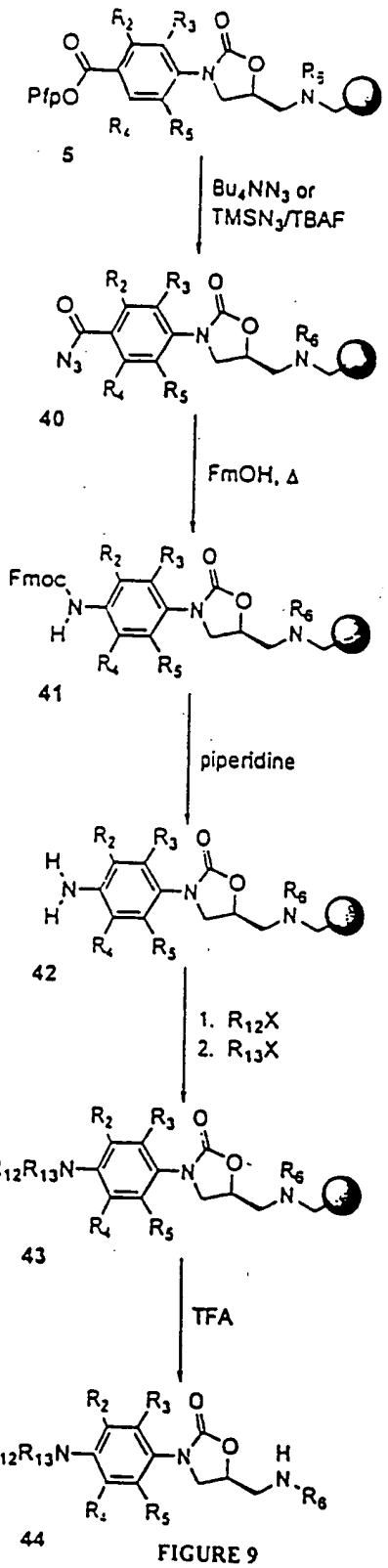

PfpO
5
Bu_4NN_3 or
$TMSN_3$/TBAF
40
FmOH, Δ
Fmoc
41
piperidine
42
1. $R_{12}X$
2. $R_{13}X$
$R_{12}R_{13}N$
43
TFA
44

FIGURE 9

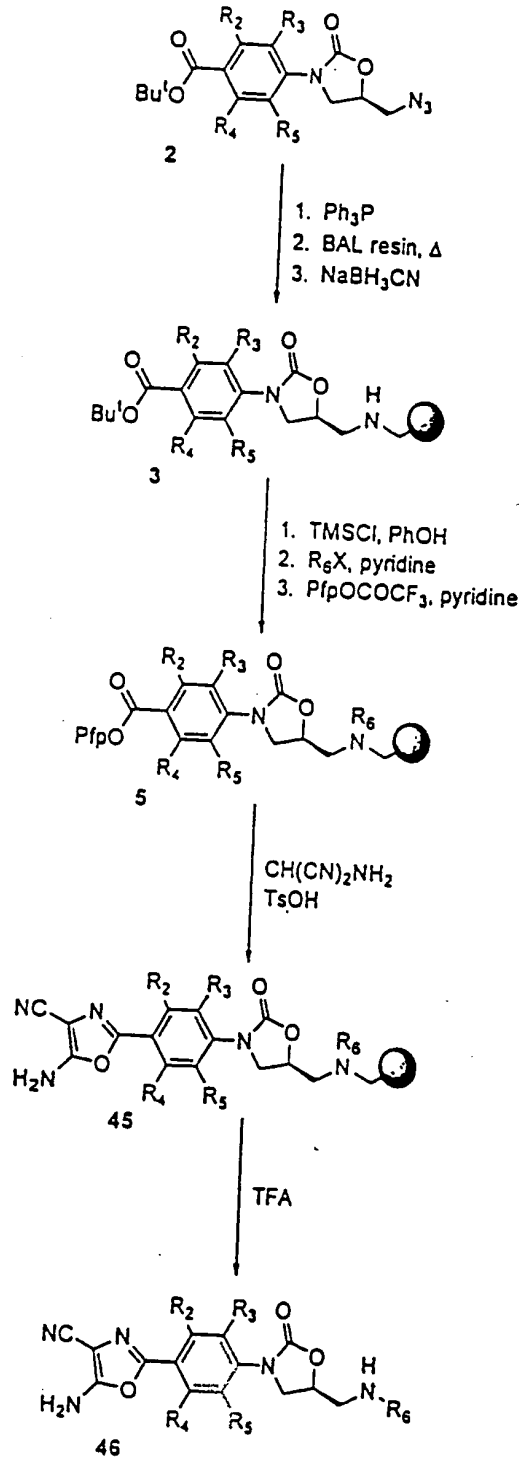

2
1. Ph3P
2. BAL resin, Δ
3. NaBH3CN
3
1. TMSCl, PhOH
2. R6X, pyridine
3. PfpOCOCF3, pyridine
5
CH(CN)2NH2
TsOH
45
TFA
46

FIGURE 10

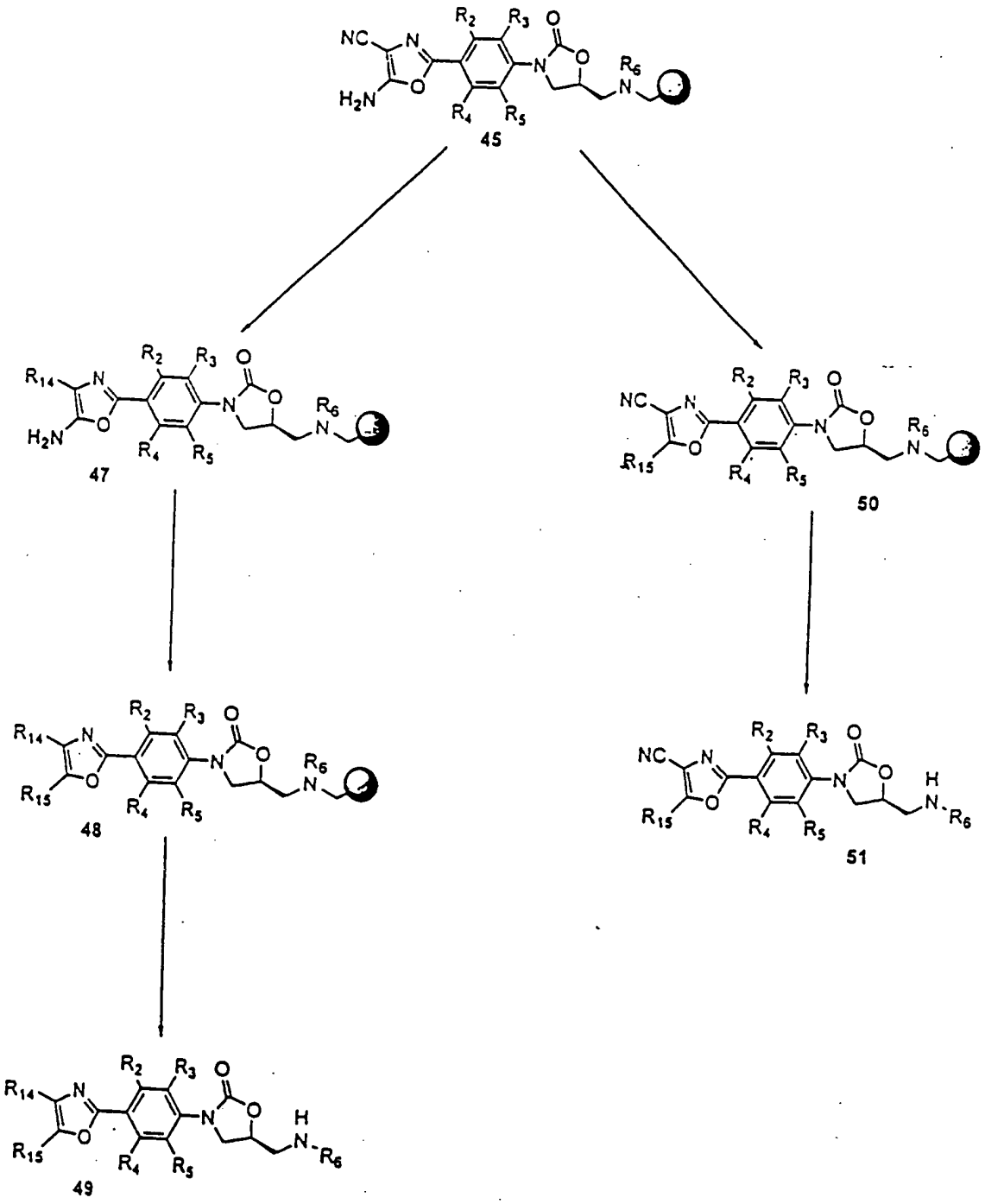


FIGURE 11

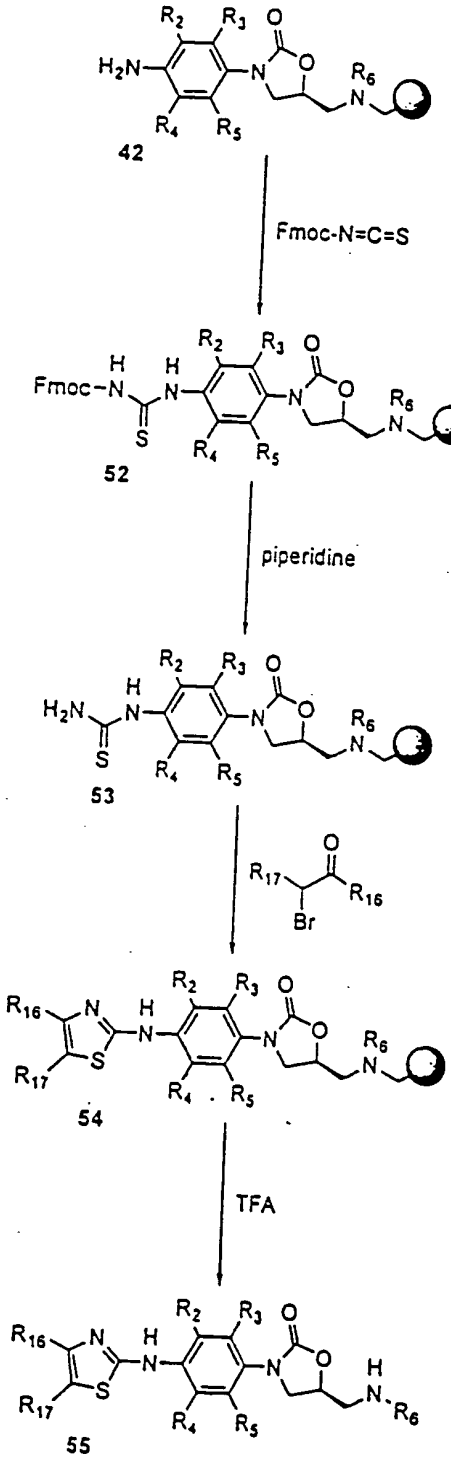
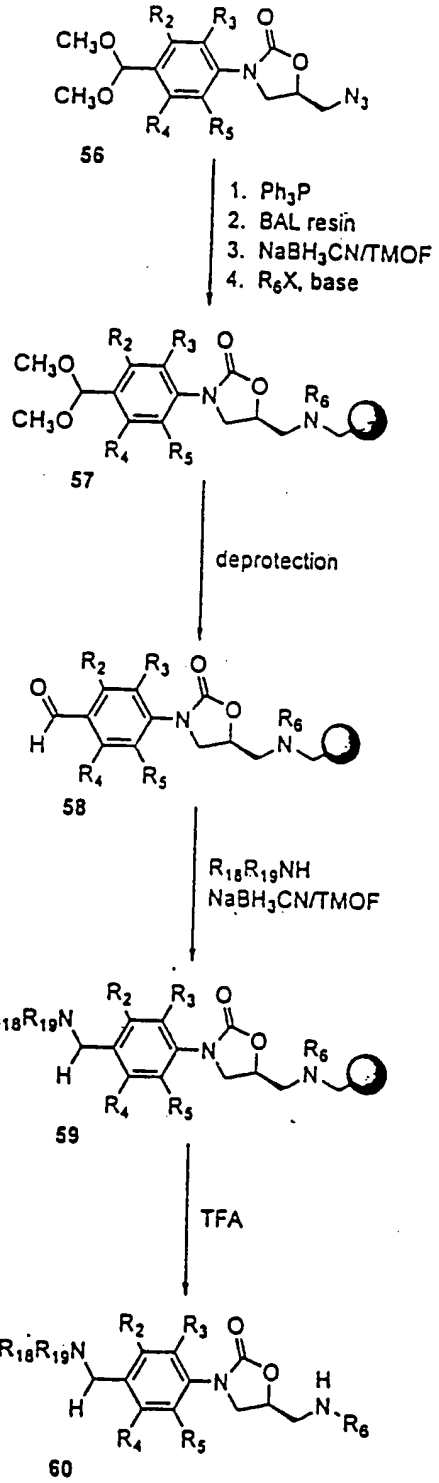


FIGURE 12



56 57 58 59 60

FIGURE 13

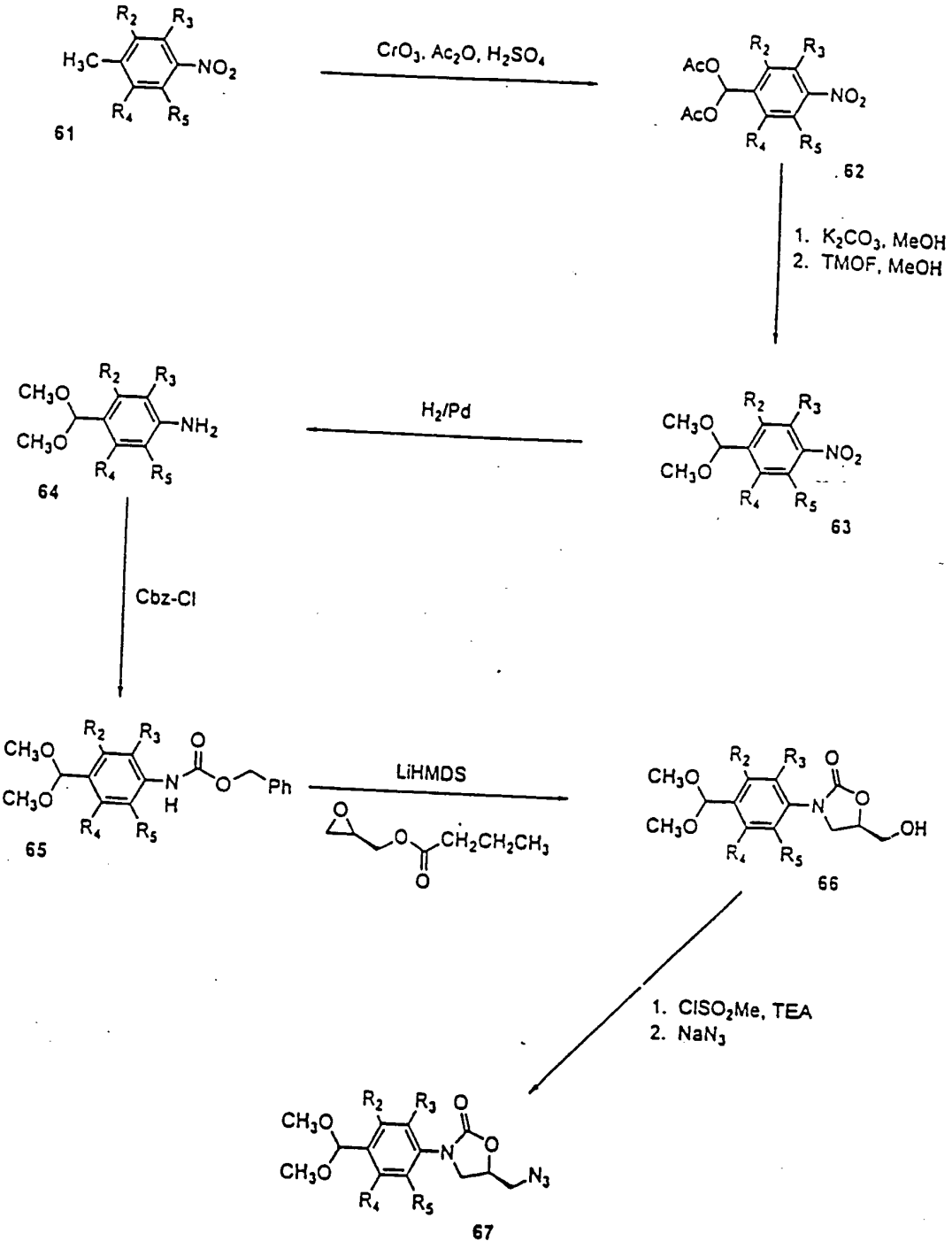

CrO_3, Ac_2O, H_2SO_4
1. K_2CO_3, MeOH
2. TMOF, MeOH
H_2/Pd
Cbz-Cl
LiHMDS
1. $ClSO_2Me$, TEA
2. NaN_3
61
62
63
64
65
66
67

FIGURE 14

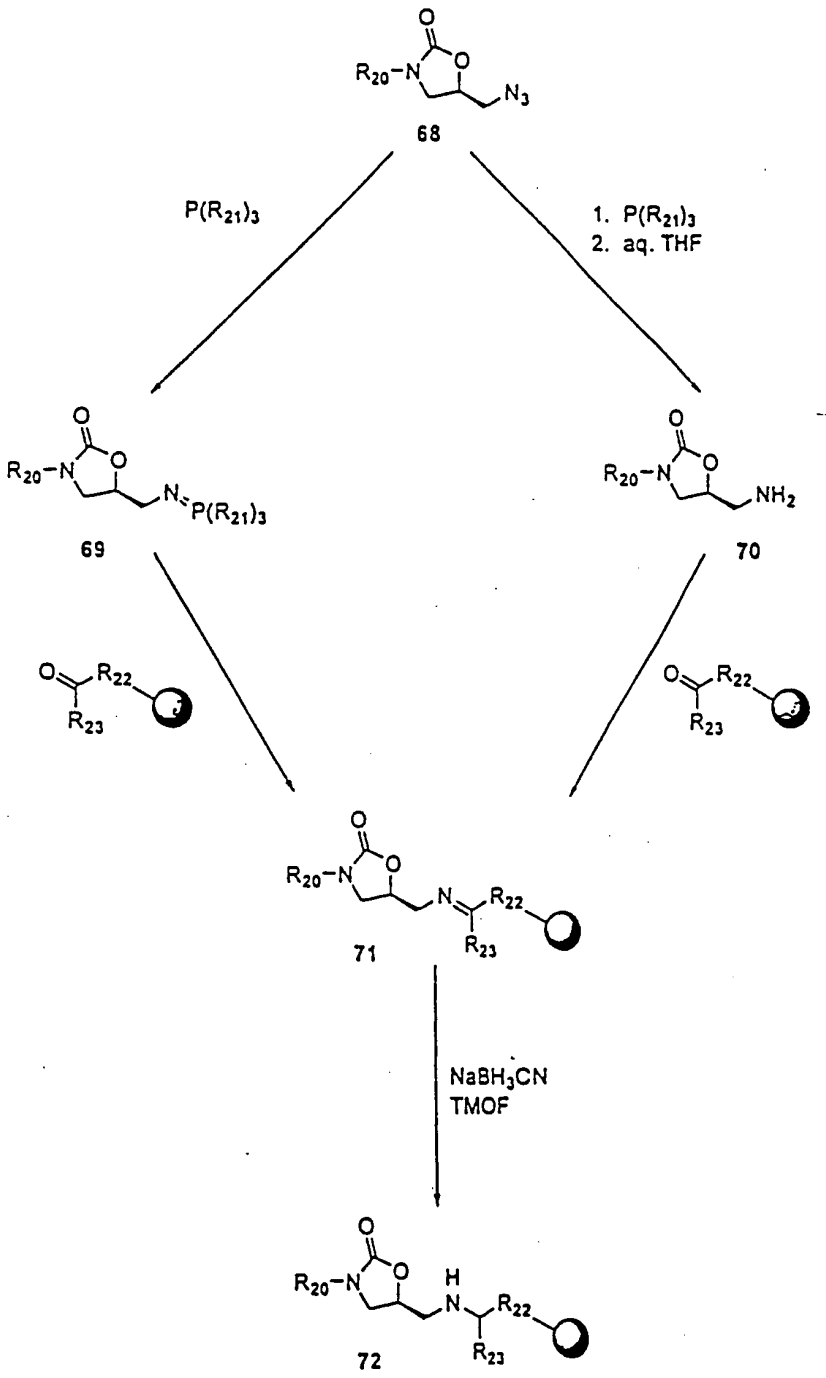


FIGURE 15

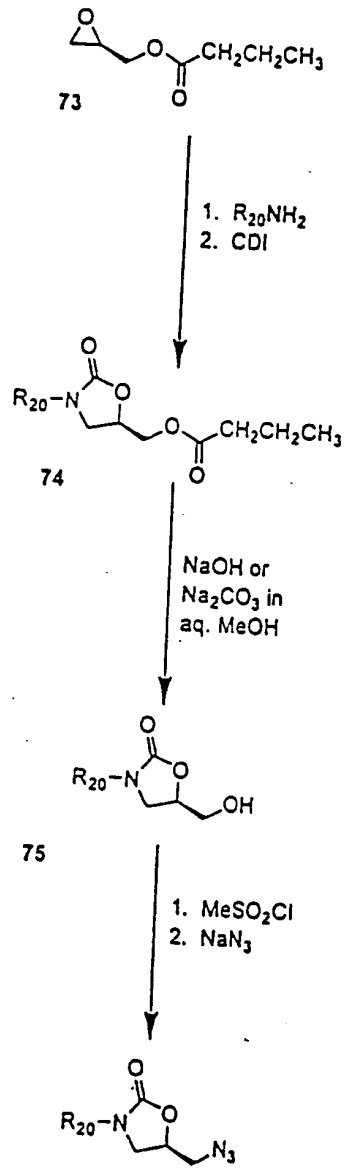
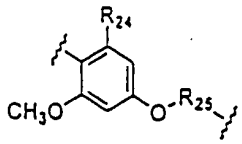

73
1. $R_{20}NH_2$
2. CDI
74
NaOH or
Na_2CO_3 in
aq. MeOH
75
1. $MeSO_2Cl$
2. NaN_3
68

FIGURE 16



76

FIGURE 17

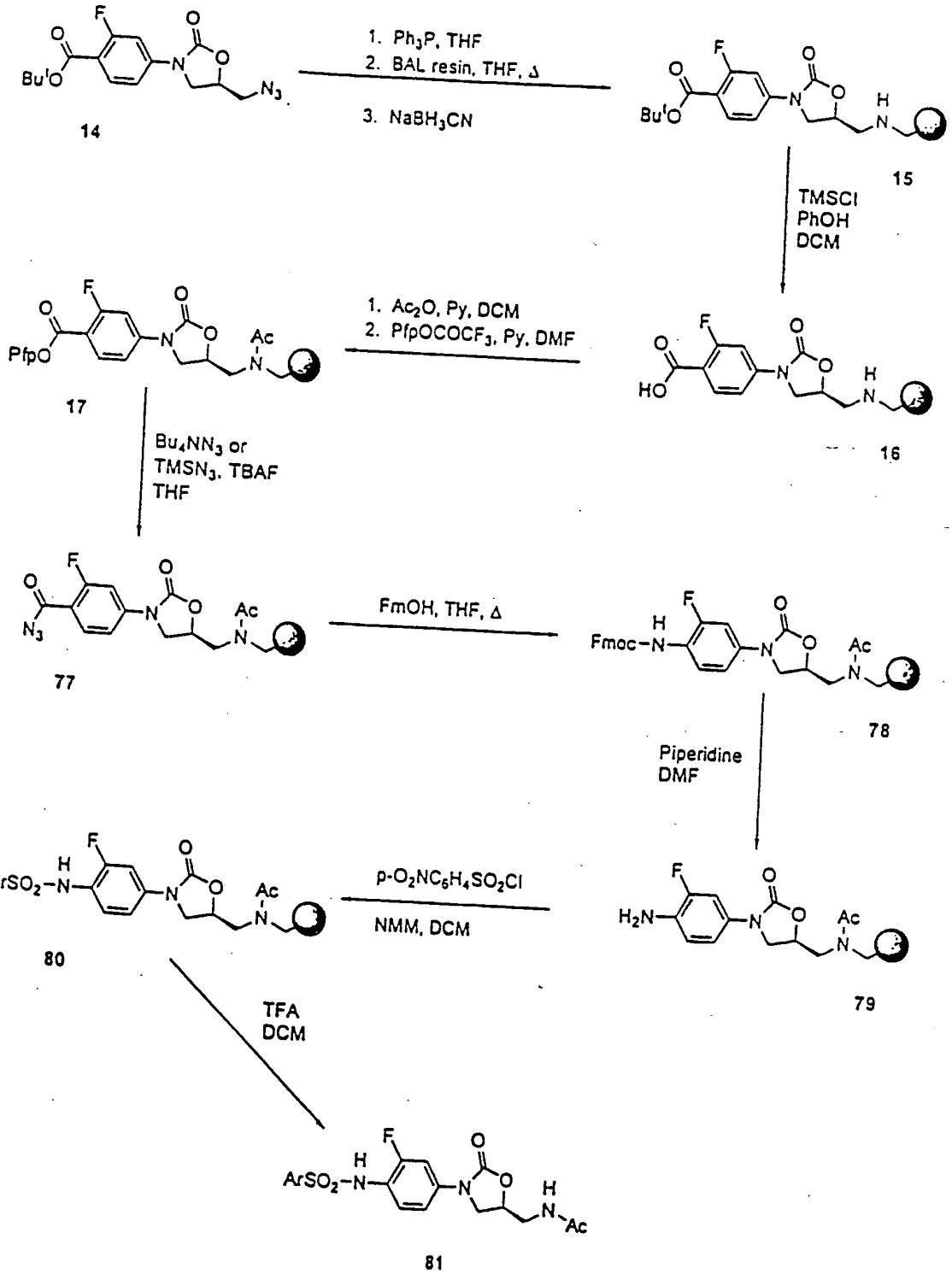

1. Ph_3P, THF
2. BAL resin, THF, Δ
3. $NaBH_3CN$
TMSCl
PhOH
DCM
1. Ac_2O, Py, DCM
2. $PfpOCOCF_3$, Py, DMF
Bu_4NN_3 or
$TMSN_3$, TBAF
THF
FmOH, THF, Δ
Piperidine
DMF
$p\text{-}O_2NC_6H_4SO_2Cl$
NMM, DCM
TFA
DCM
14
15
16
17
77
78
79
80
81

FIGURE 18

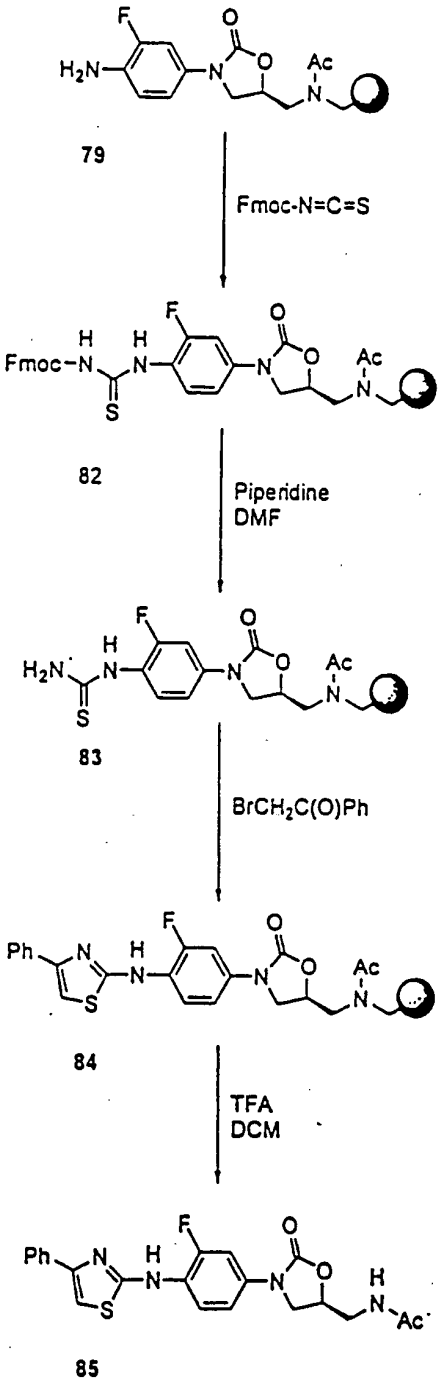


FIGURE 19

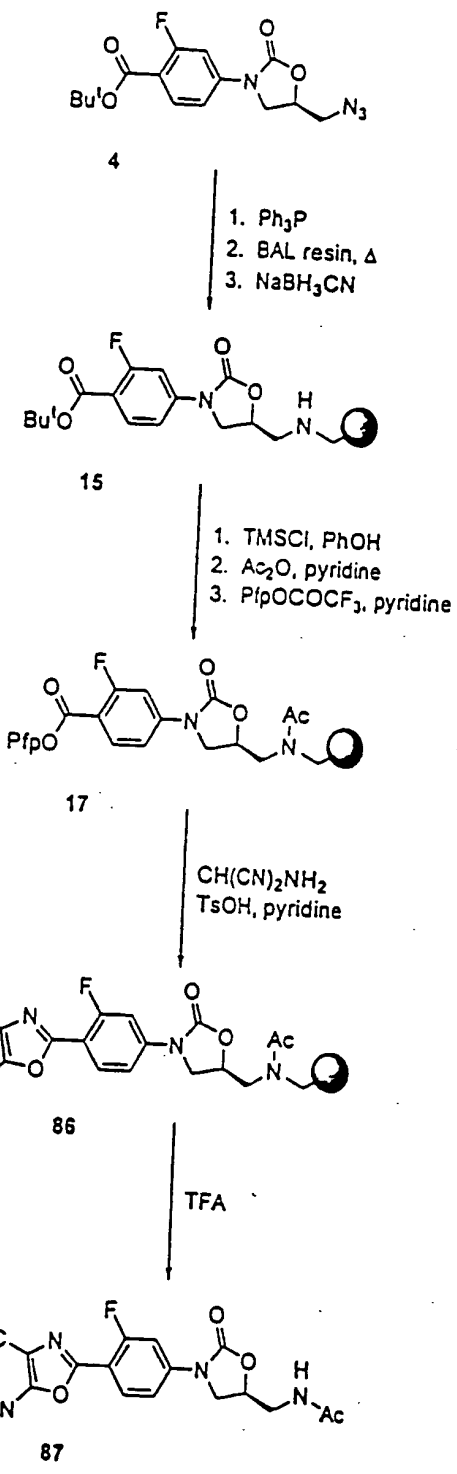

F
O
Bu^{t}O
N$_3$
4
1. Ph$_3$P
2. BAL resin, Δ
3. NaBH$_3$CN
H
15
1. TMSCl, PhOH
2. Ac$_2$O, pyridine
3. PfpOCOCF$_3$, pyridine
PfpO
Ac
17
CH(CN)$_2$NH$_2$
TsOH, pyridine
NC
H$_2$N
86
TFA
87

FIGURE 20

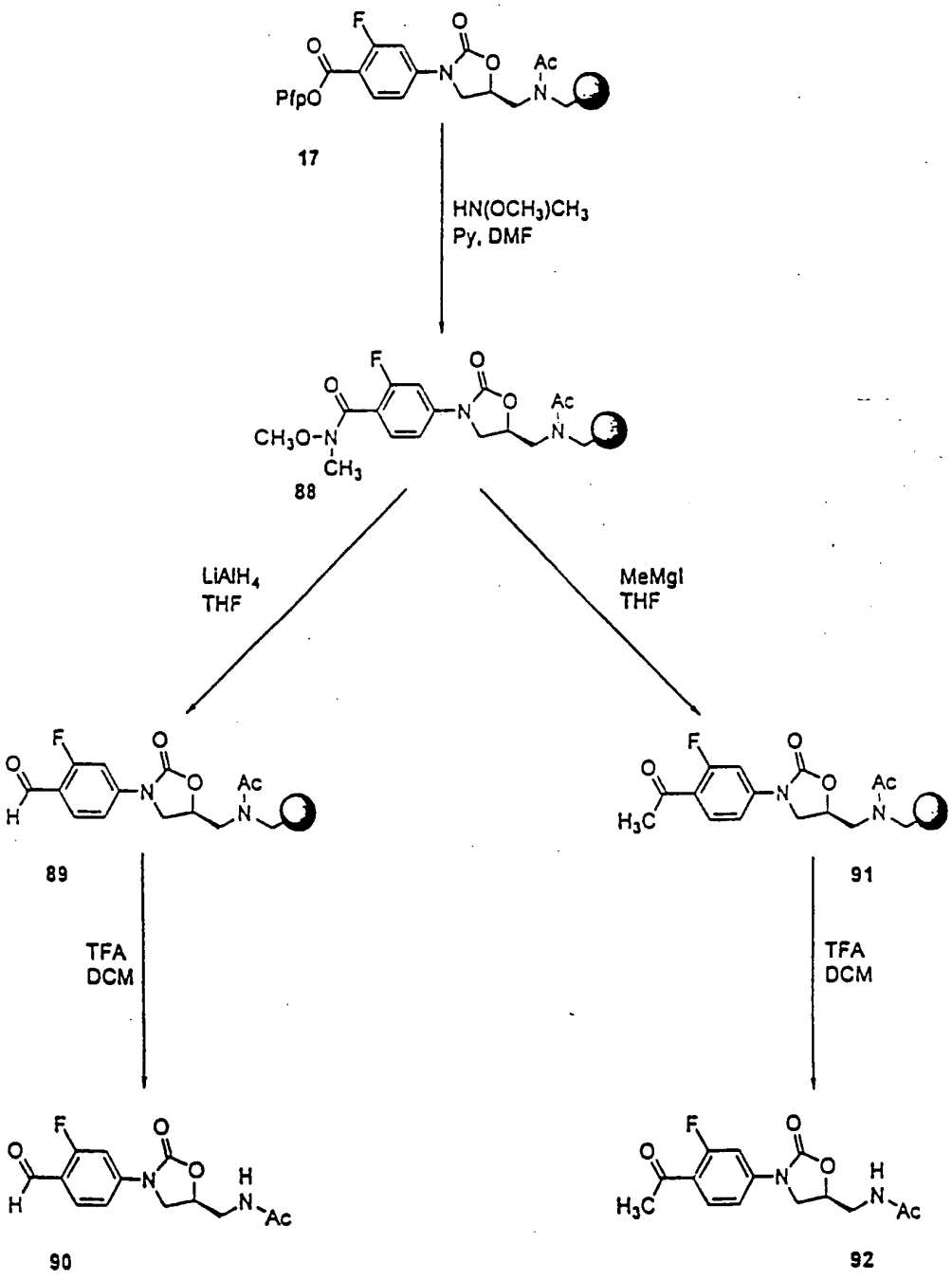

PfpO
17
HN(OCH3)CH3
Py, DMF
CH3O-N
CH3
88
LiAlH4
THF
MeMgI
THF
89
91
TFA
DCM
TFA
DCM
90
92

FIGURE 21

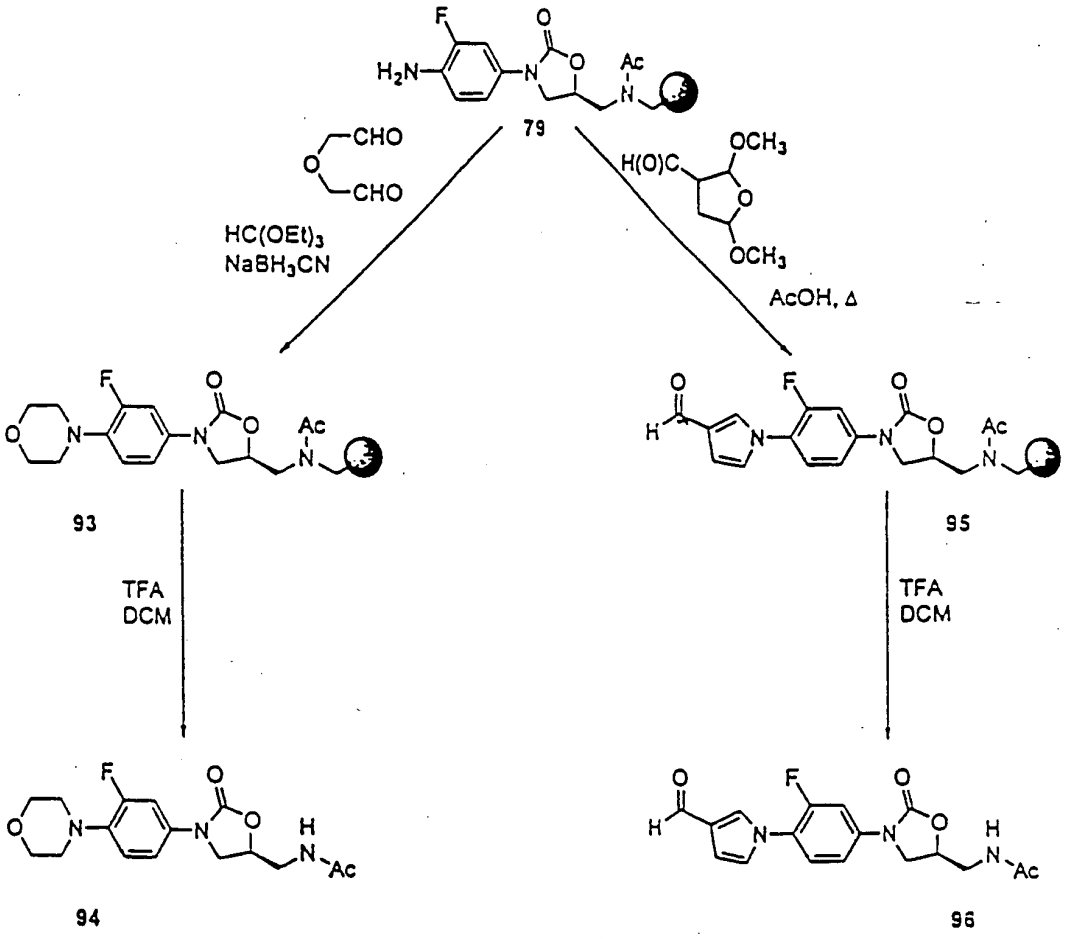


FIGURE 22

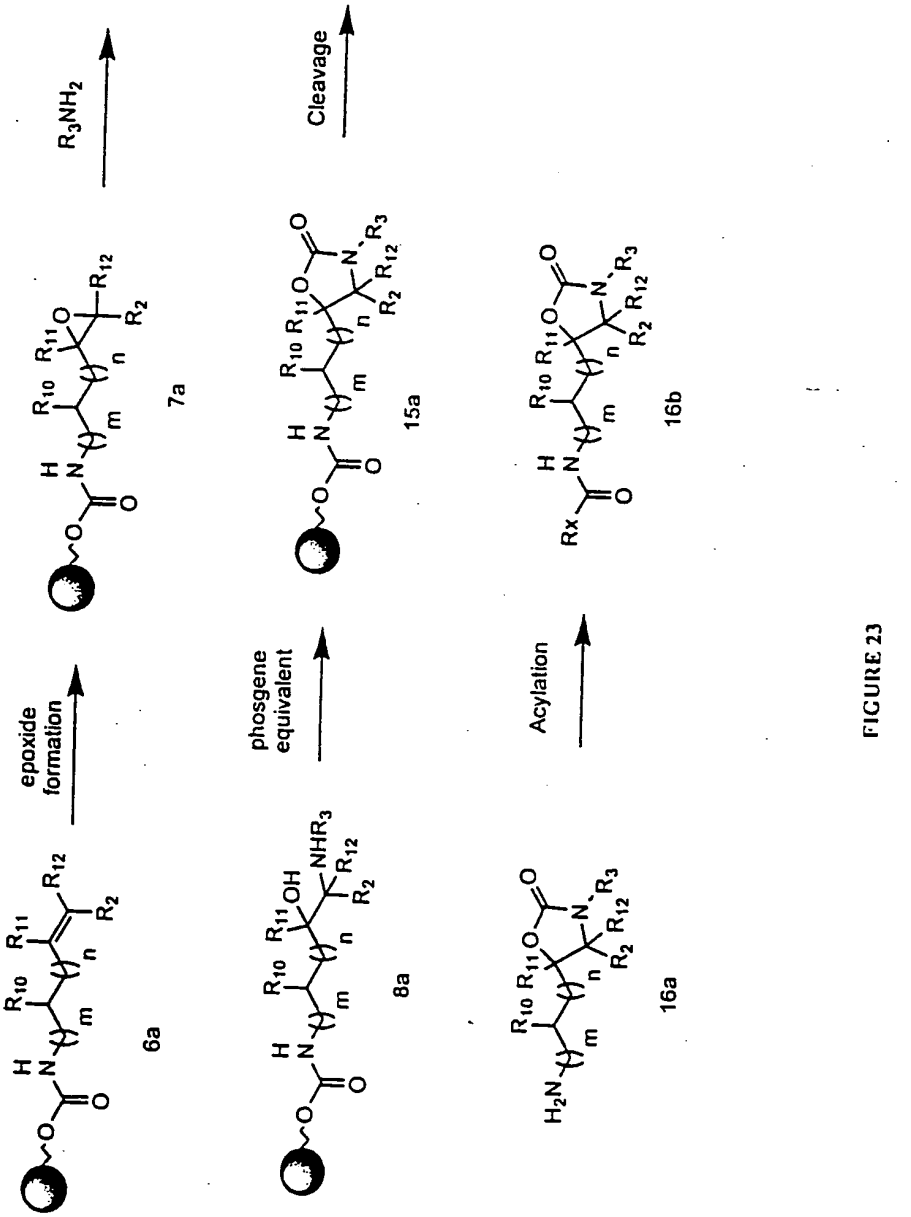

epoxide formation
phosgene equivalent
Acylation
Cleavage
R_3NH_2
6a
7a
8a
15a
16a
16b

FIGURE 23

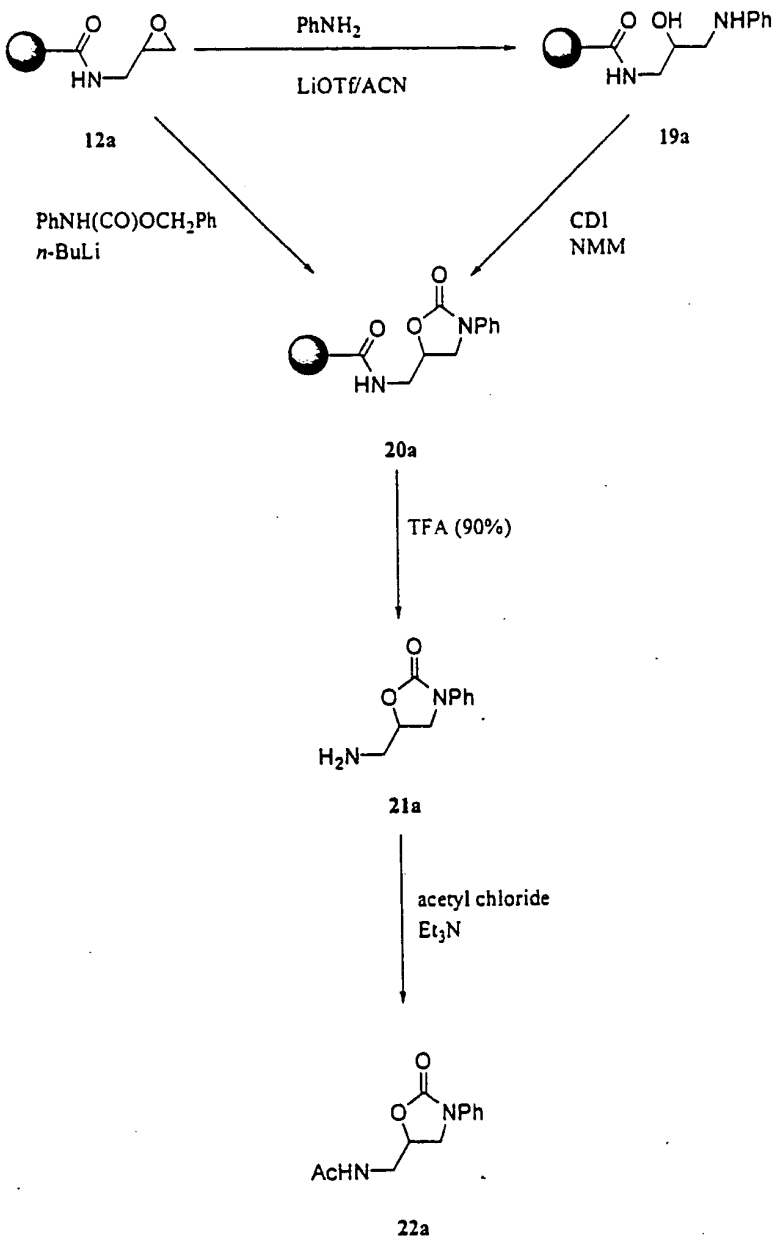

PhNH2
LiOTf/ACN
12a
19a
PhNH(CO)OCH2Ph
n-BuLi
CDI
NMM
20a
TFA (90%)
21a
acetyl chloride
Et3N
22a

FIGURE 24

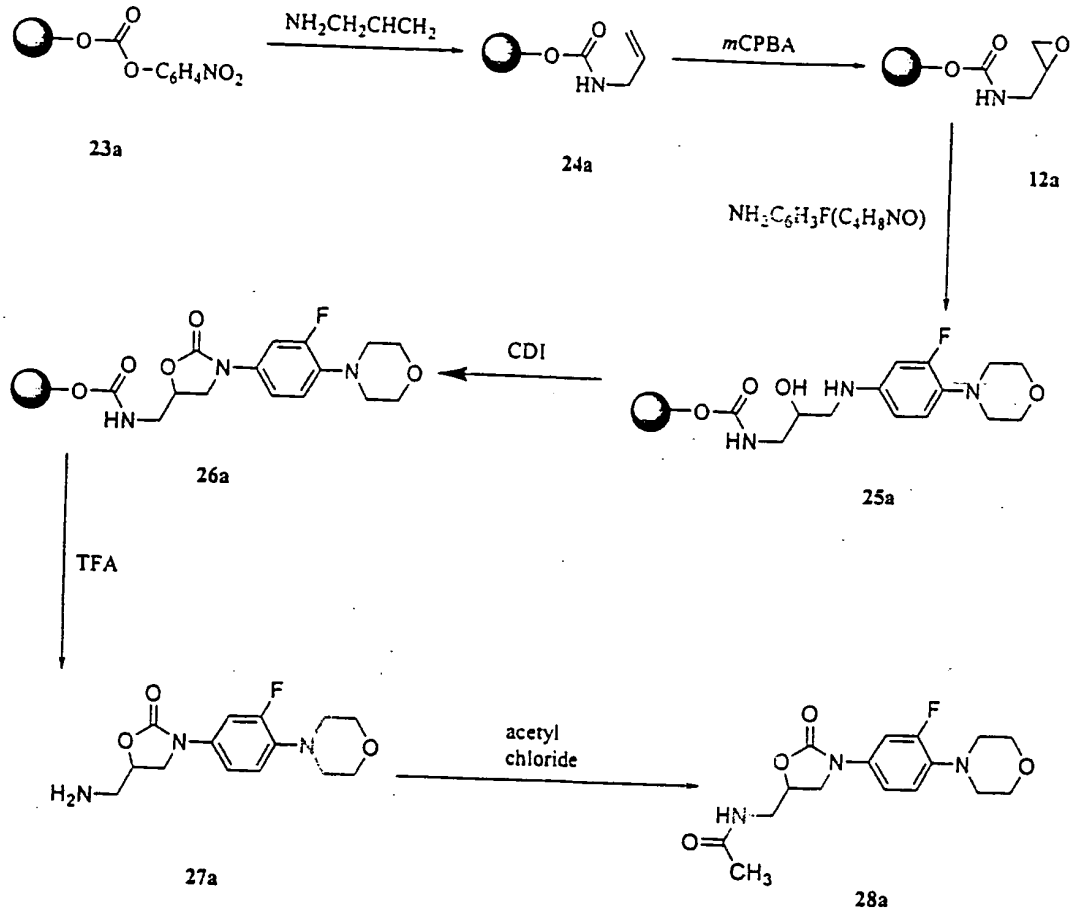

NH2CH2CHCH2
mCPBA
NH2C6H3F(C4H8NO)
CDI
TFA
acetyl chloride
23a
24a
12a
25a
26a
27a
28a

FIGURE 25

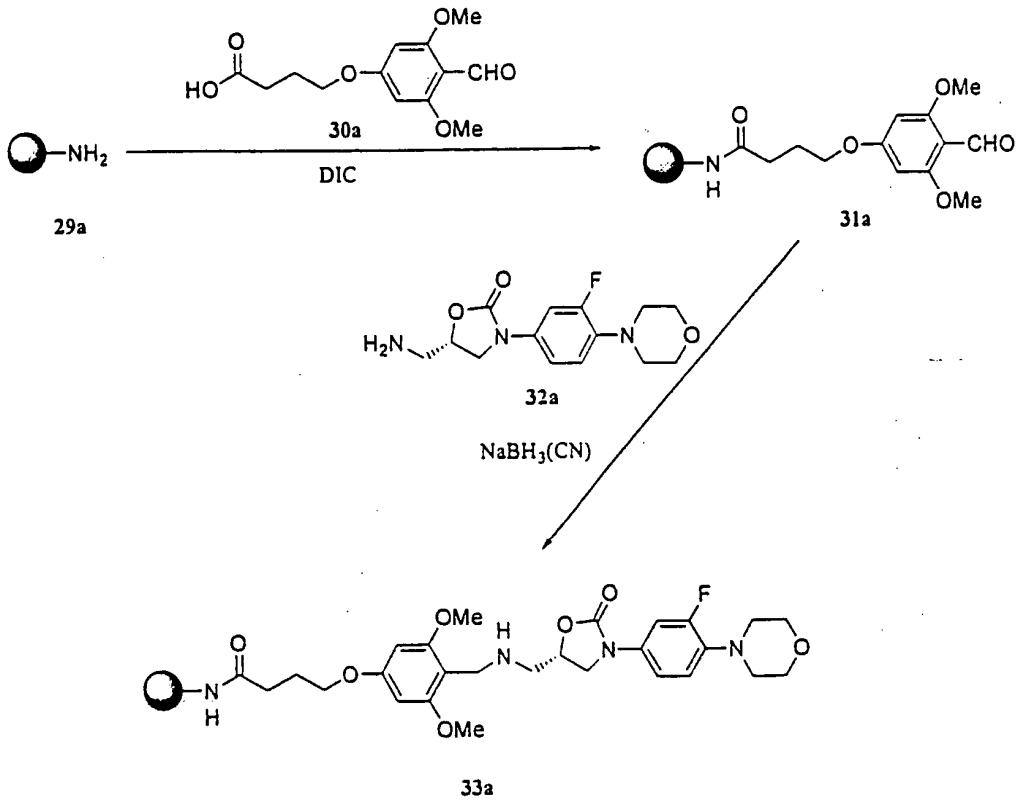

OMe
O
HO
CHO
O
OMe
30a
NH2
DIC
29a
O
N
H
O
OMe
CHO
OMe
31a
F
O
O
N
H2N
N
O
32a
NaBH3(CN)
OMe
H
N
O
F
O
N
N
O
O
N
H
OMe
33a

FIGURE 26

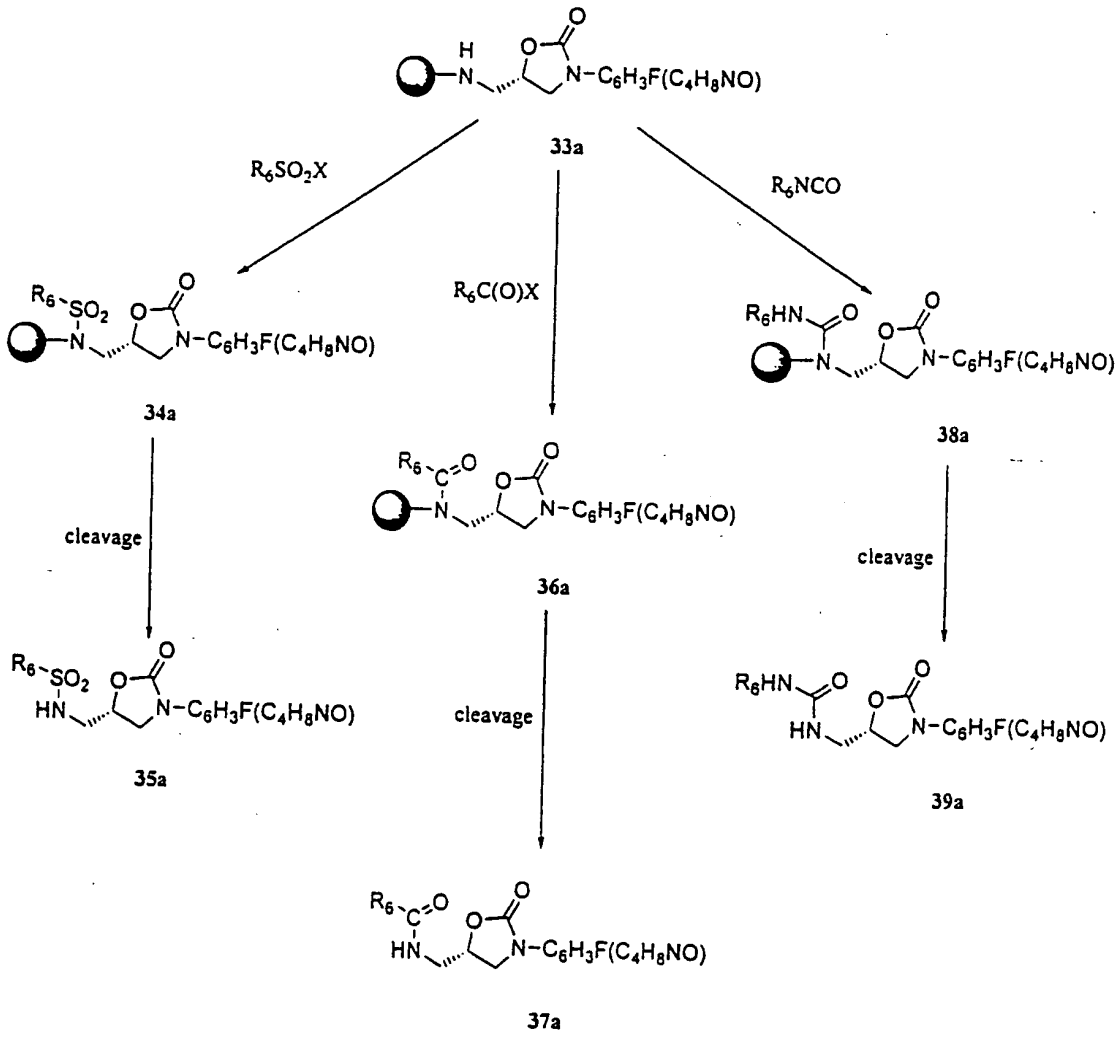

33a
R_6SO_2X
$R_6C(O)X$
R_6NCO
34a
36a
38a
cleavage
cleavage
cleavage
35a
37a
39a

FIGURE 27

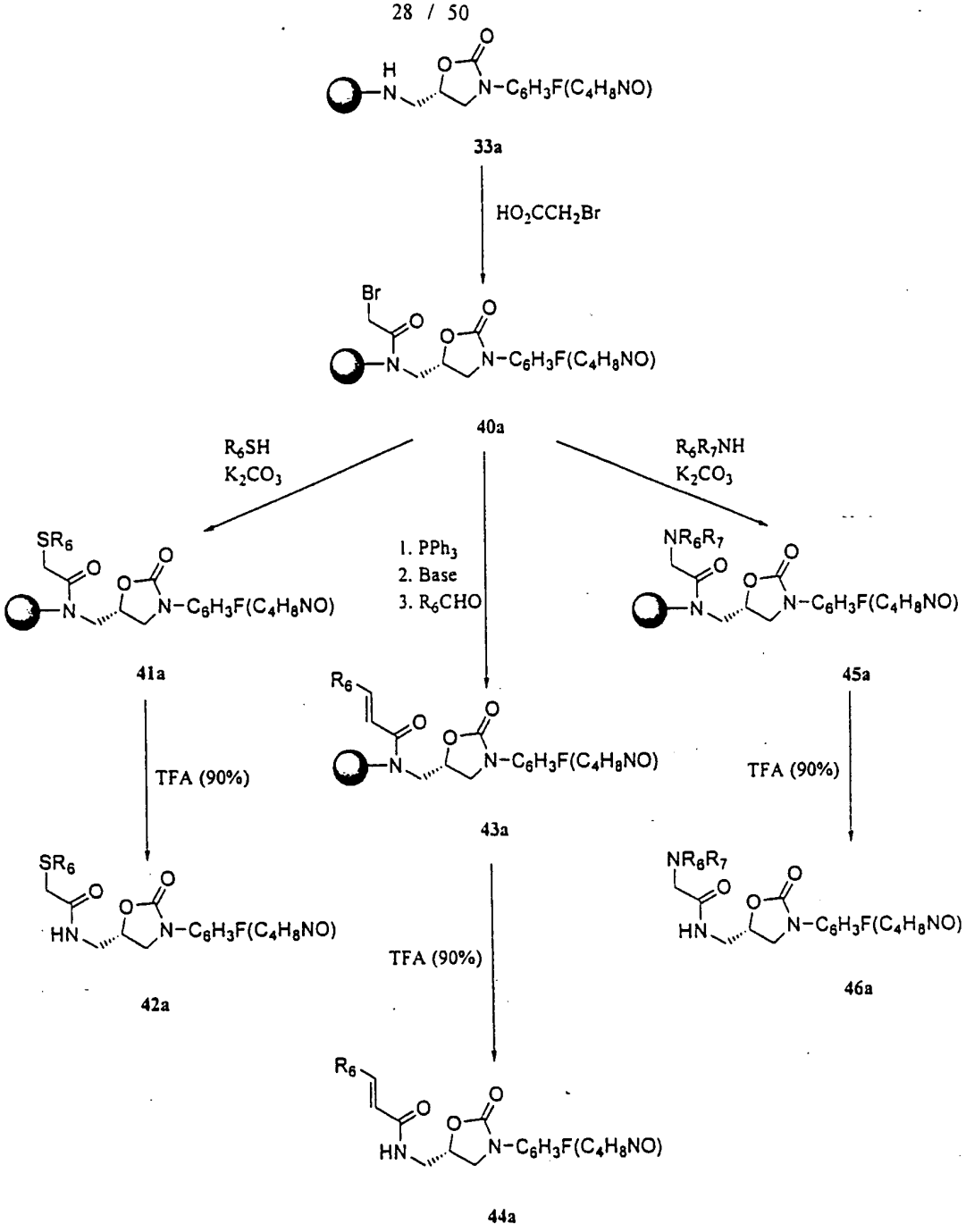

33a
HO2CCH2Br
40a
R6SH
K2CO3
R6R7NH
K2CO3
1. PPh3
2. Base
3. R6CHO
41a
45a
43a
TFA (90%)
TFA (90%)
TFA (90%)
42a
46a
44a

FIGURE 28

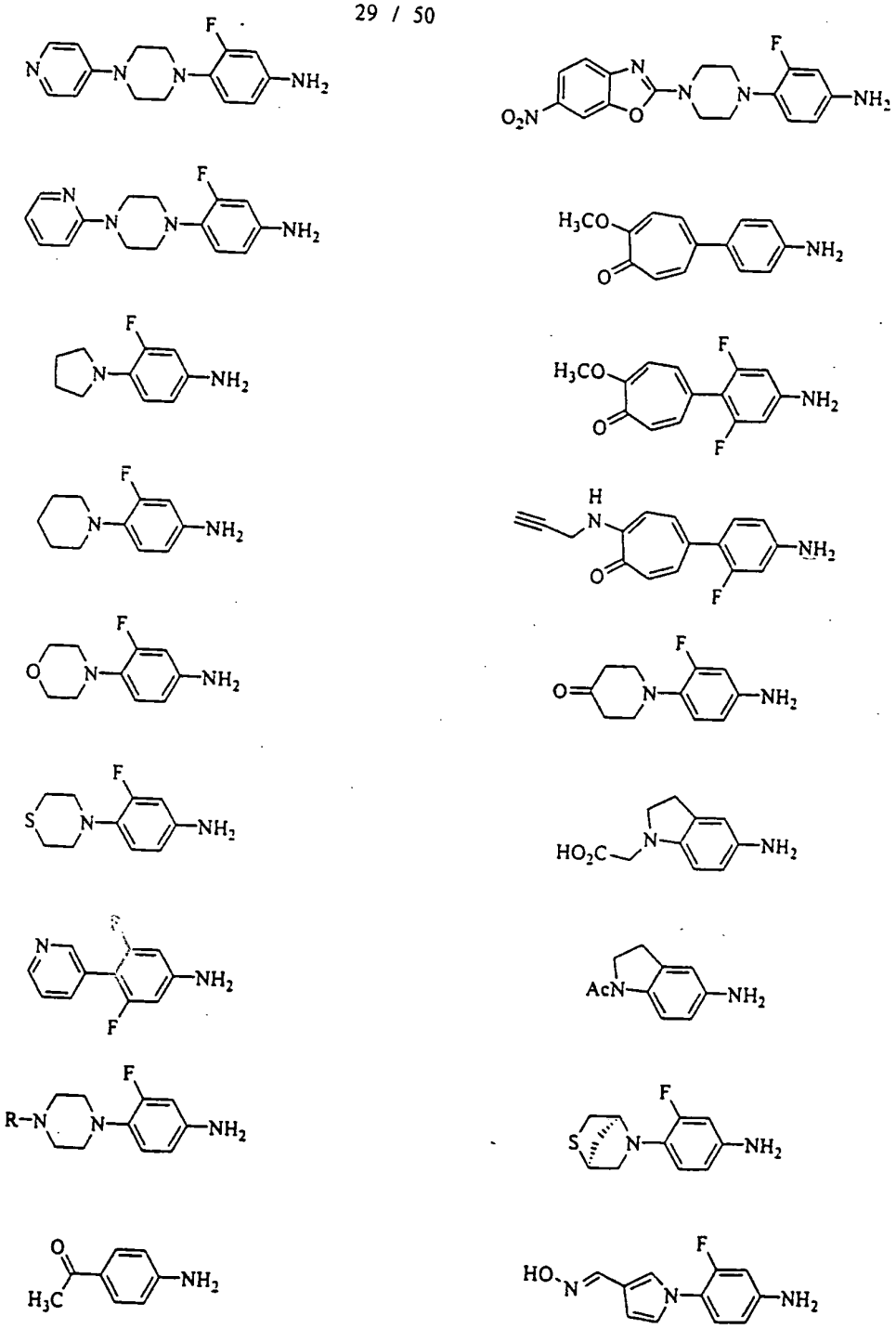
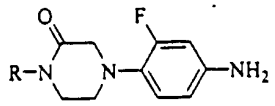
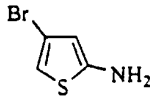
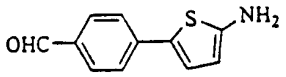
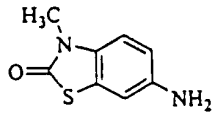
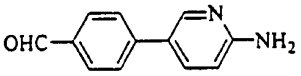
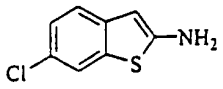
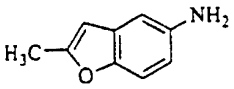
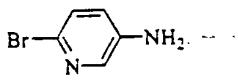
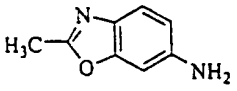
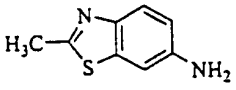
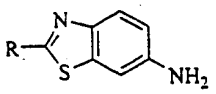
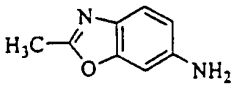
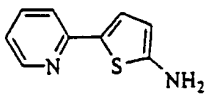
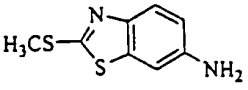
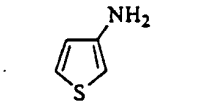


FIGURE 29

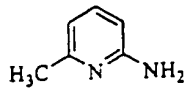
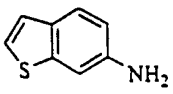
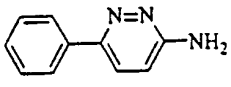




FIGURE 30

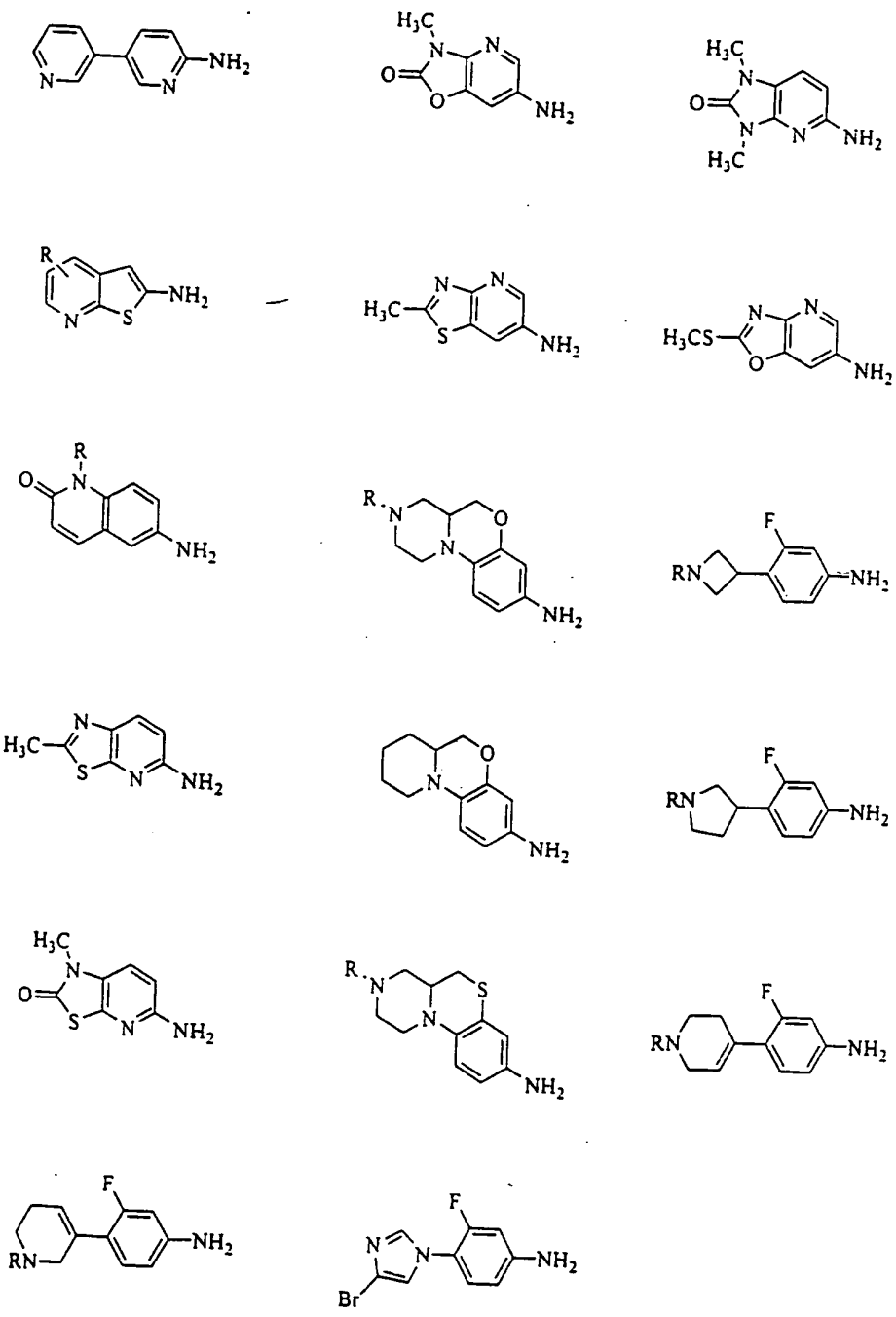
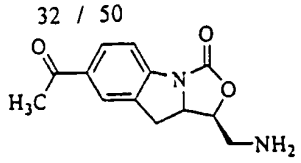
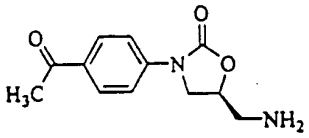
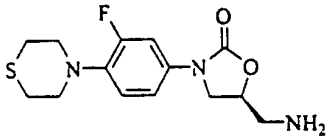
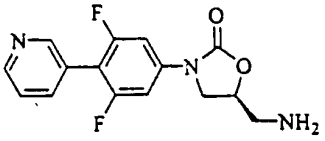


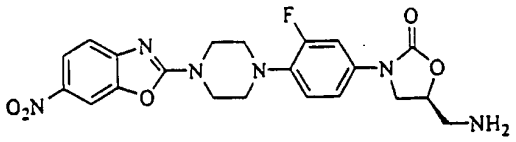
FIGURE 31











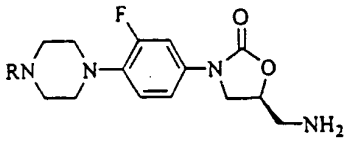


FIGURE 32

FIGURE 33

FIGURE 34

FIGURE 35

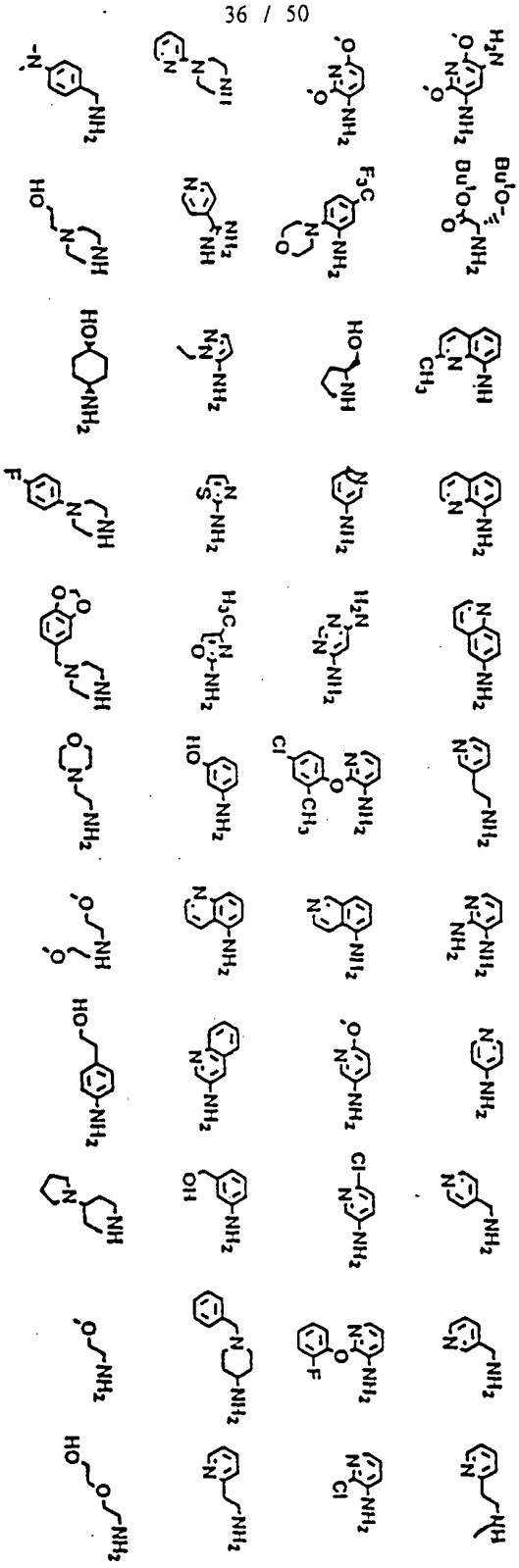


FIGURE 36

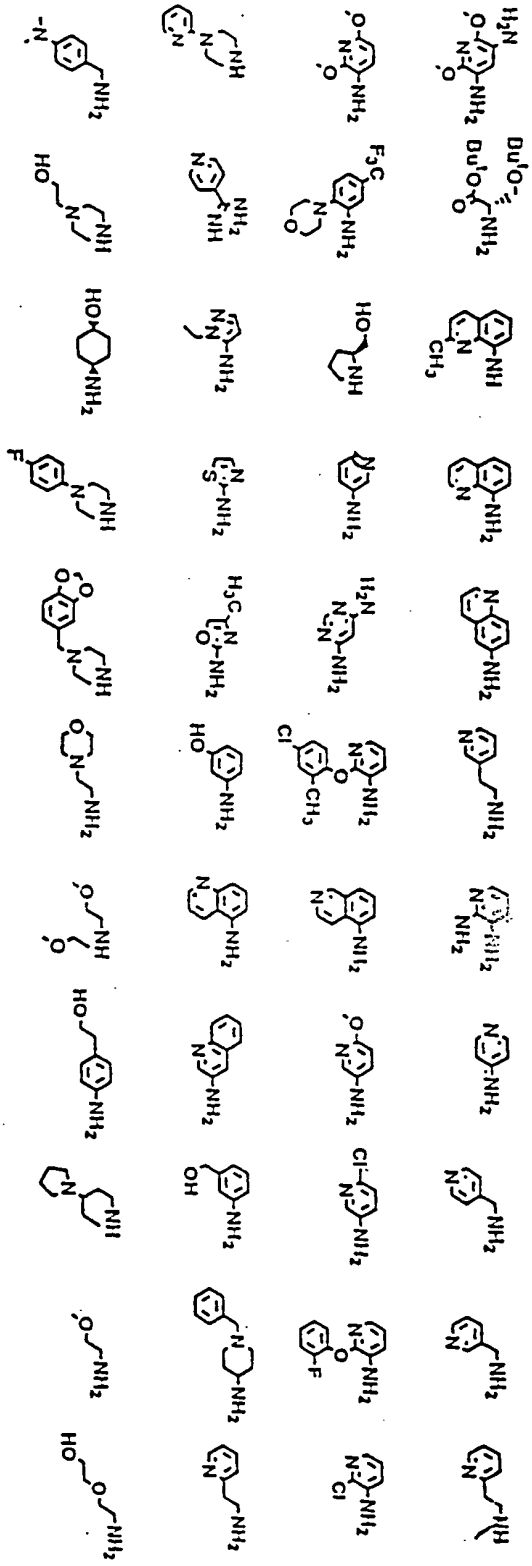
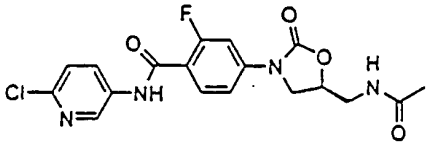
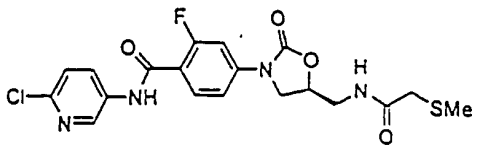
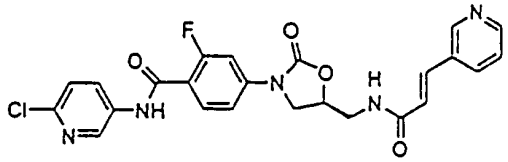
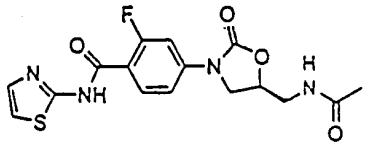


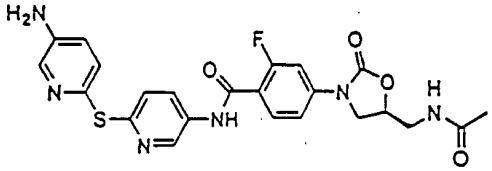
FIGURE 37

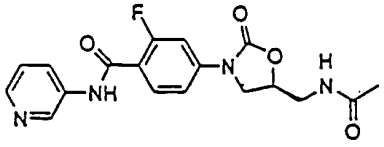


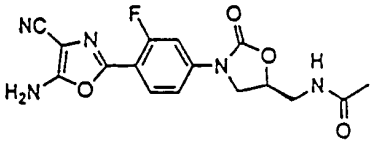












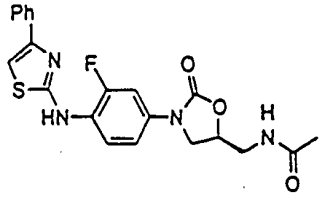


FIGURE 38

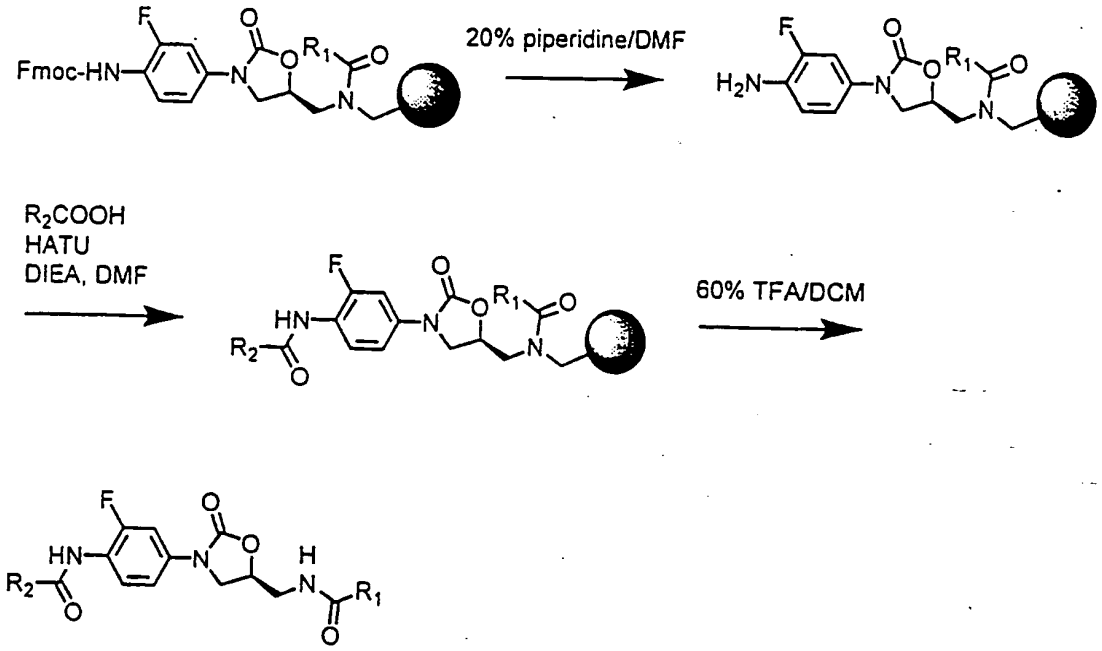

Fmoc-HN
F
O
O
R_1
O
N
O
N
20% piperidine/DMF
H_2N
R_2COOH
HATU
DIEA, DMF
HN
R_2
60% TFA/DCM
H

FIGURE 39

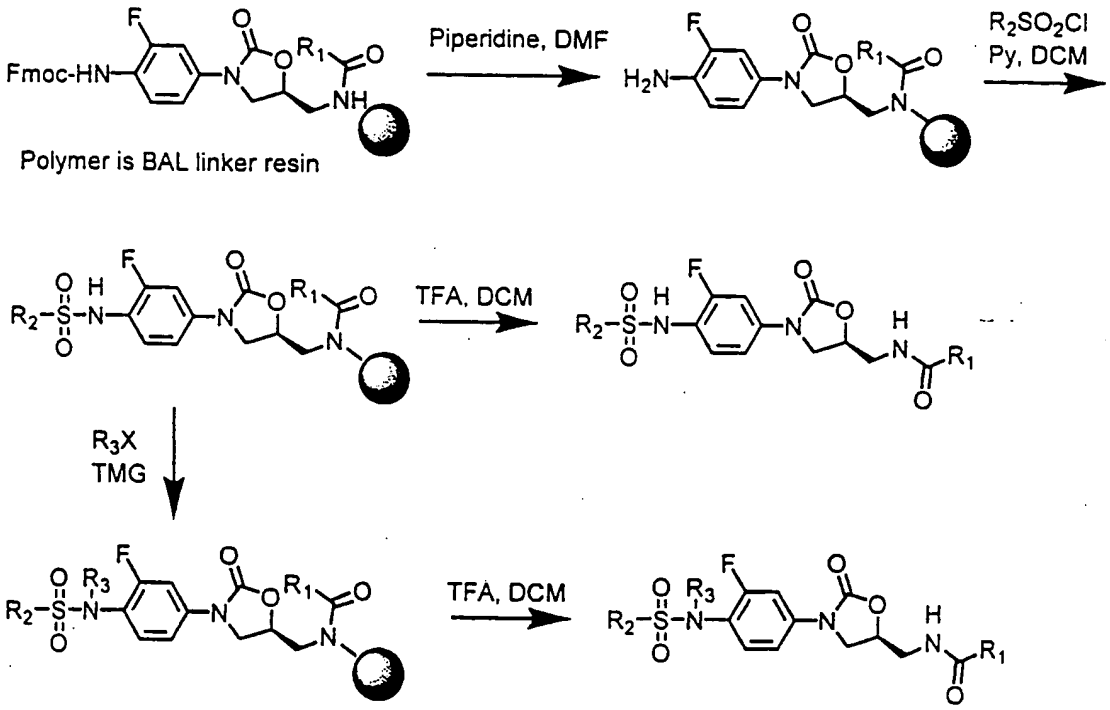

Fmoc-HN
Piperidine, DMF
H_2N
R_2SO_2Cl
Py, DCM
Polymer is BAL linker resin
TFA, DCM
R_3X
TMG
TFA, DCM

FIGURE 40

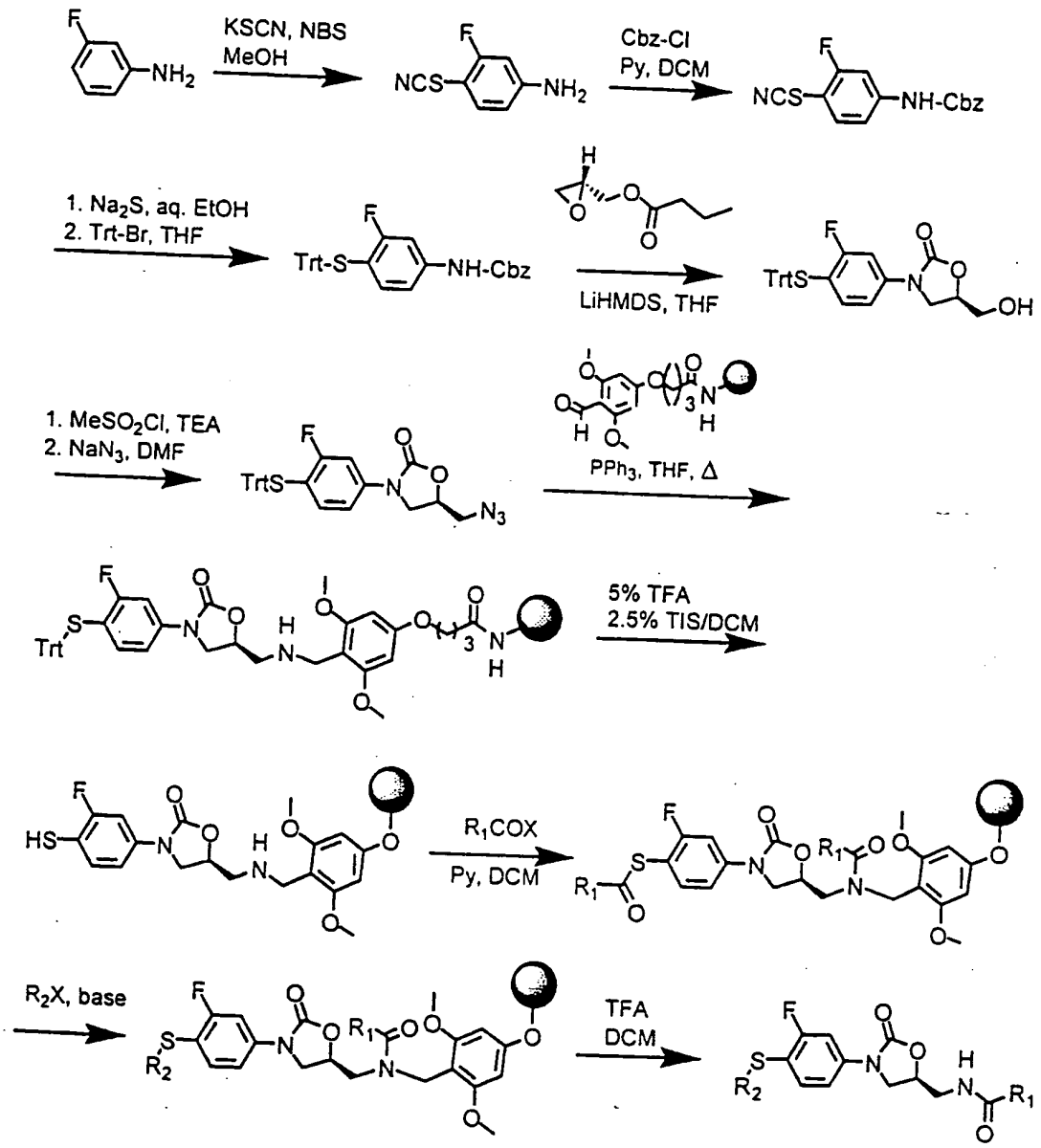

KSCN, NBS
MeOH
Cbz-Cl
Py, DCM
1. Na_2S, aq. EtOH
2. Trt-Br, THF
LiHMDS, THF
1. $MeSO_2Cl$, TEA
2. NaN_3, DMF
PPh_3, THF, Δ
5% TFA
2.5% TIS/DCM
R_1COX
Py, DCM
R_2X, base
TFA
DCM

FIGURE 41

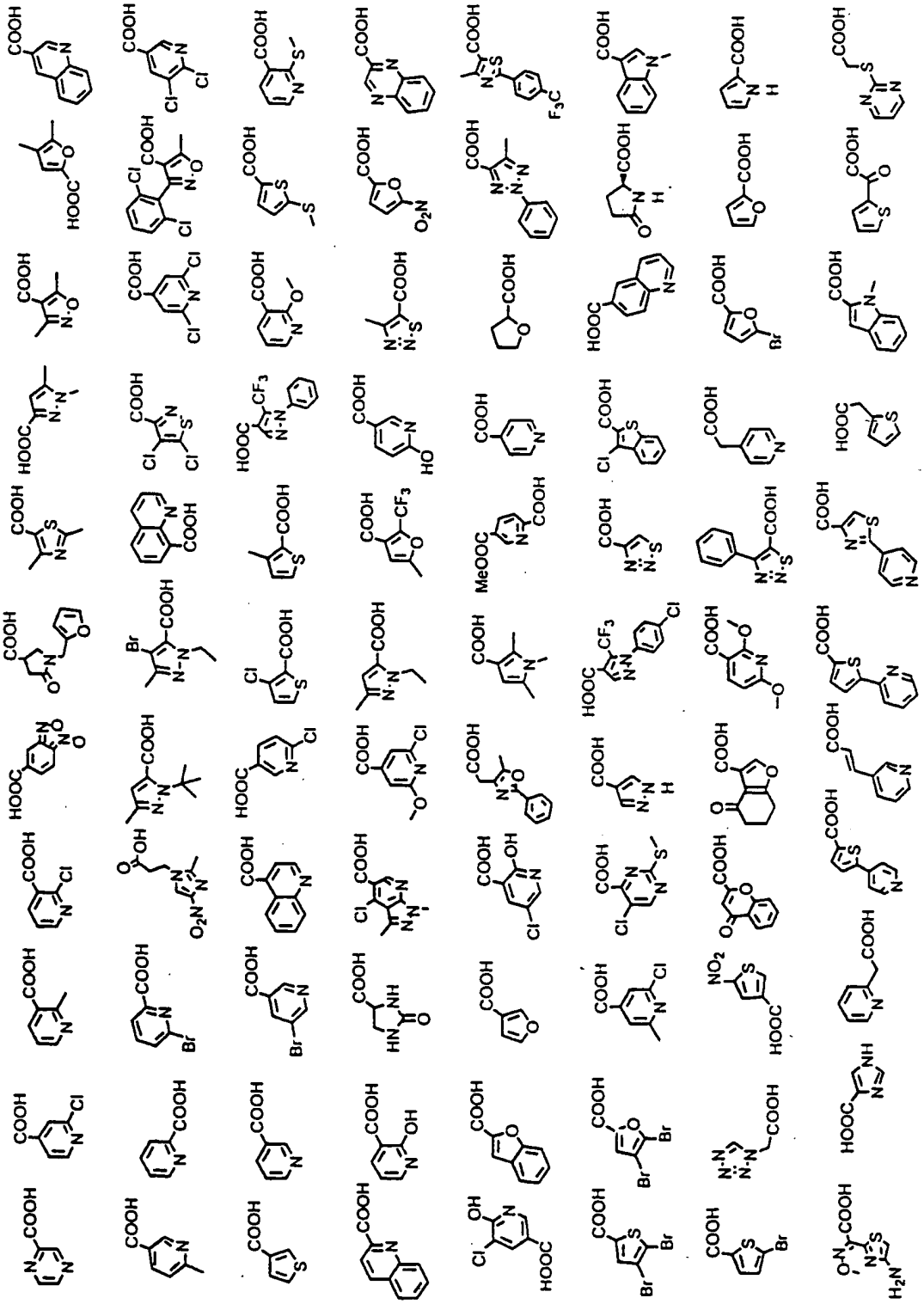


FIGURE 42

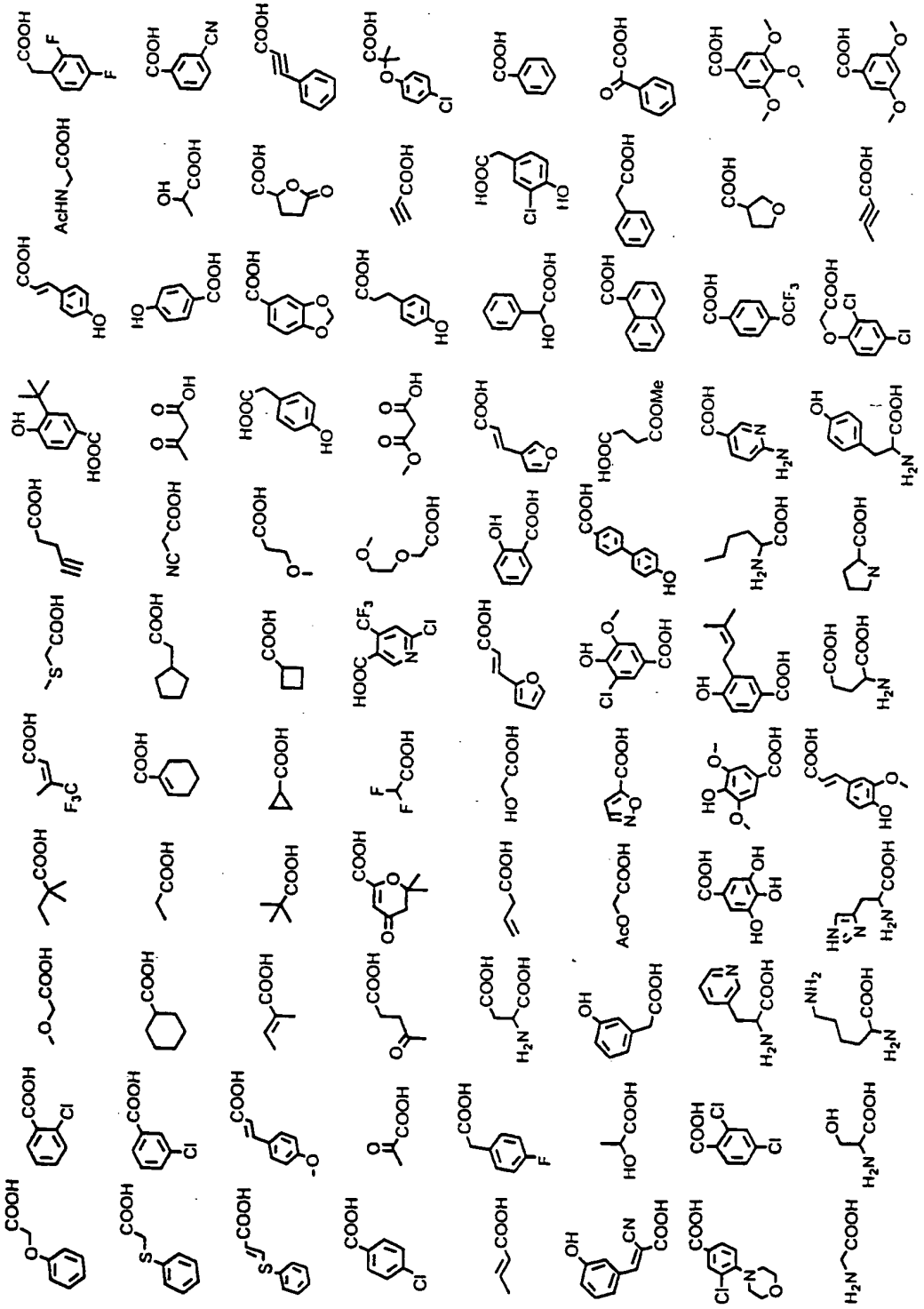


FIGURE 43

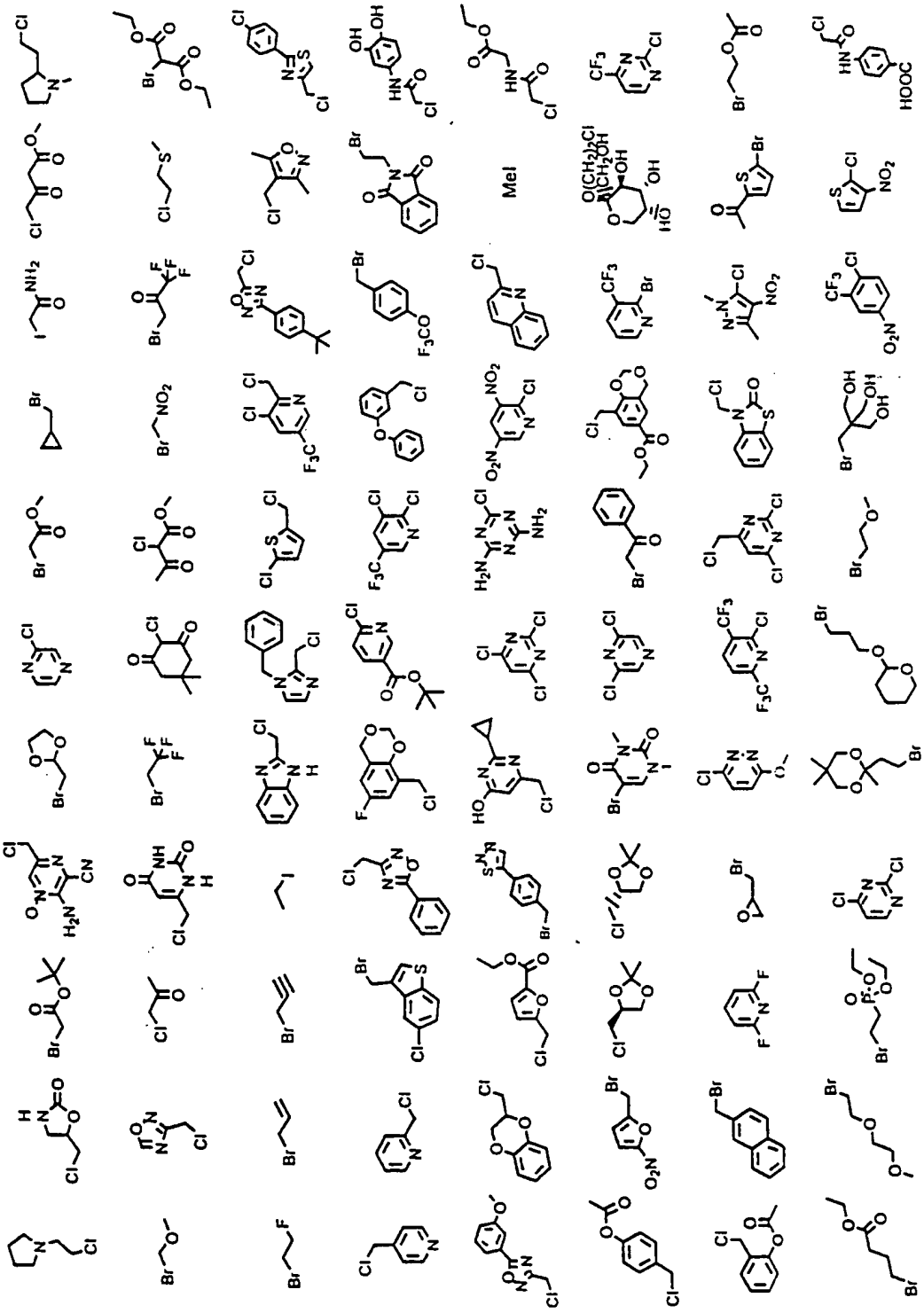


FIGURE 44

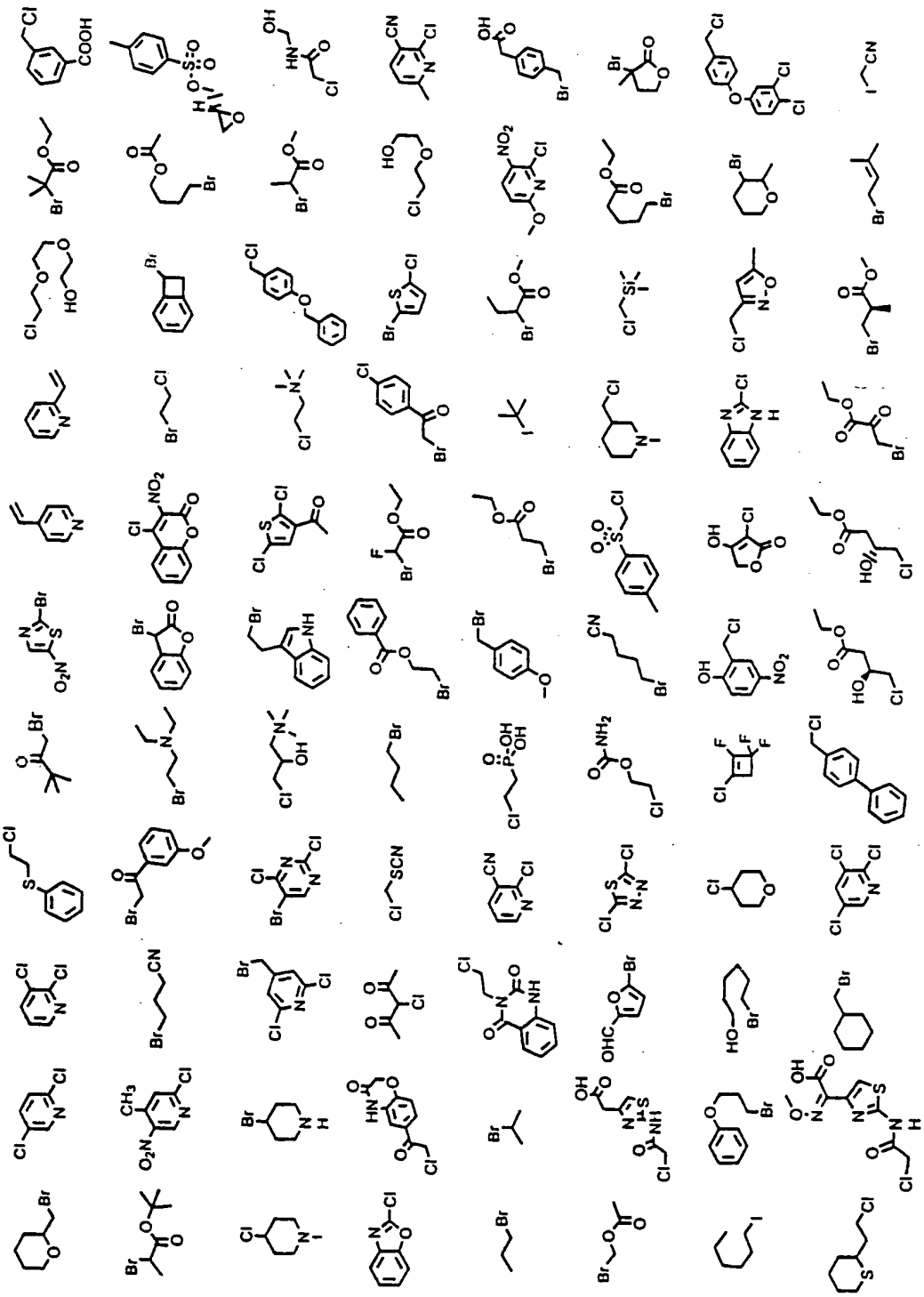


FIGURE 45

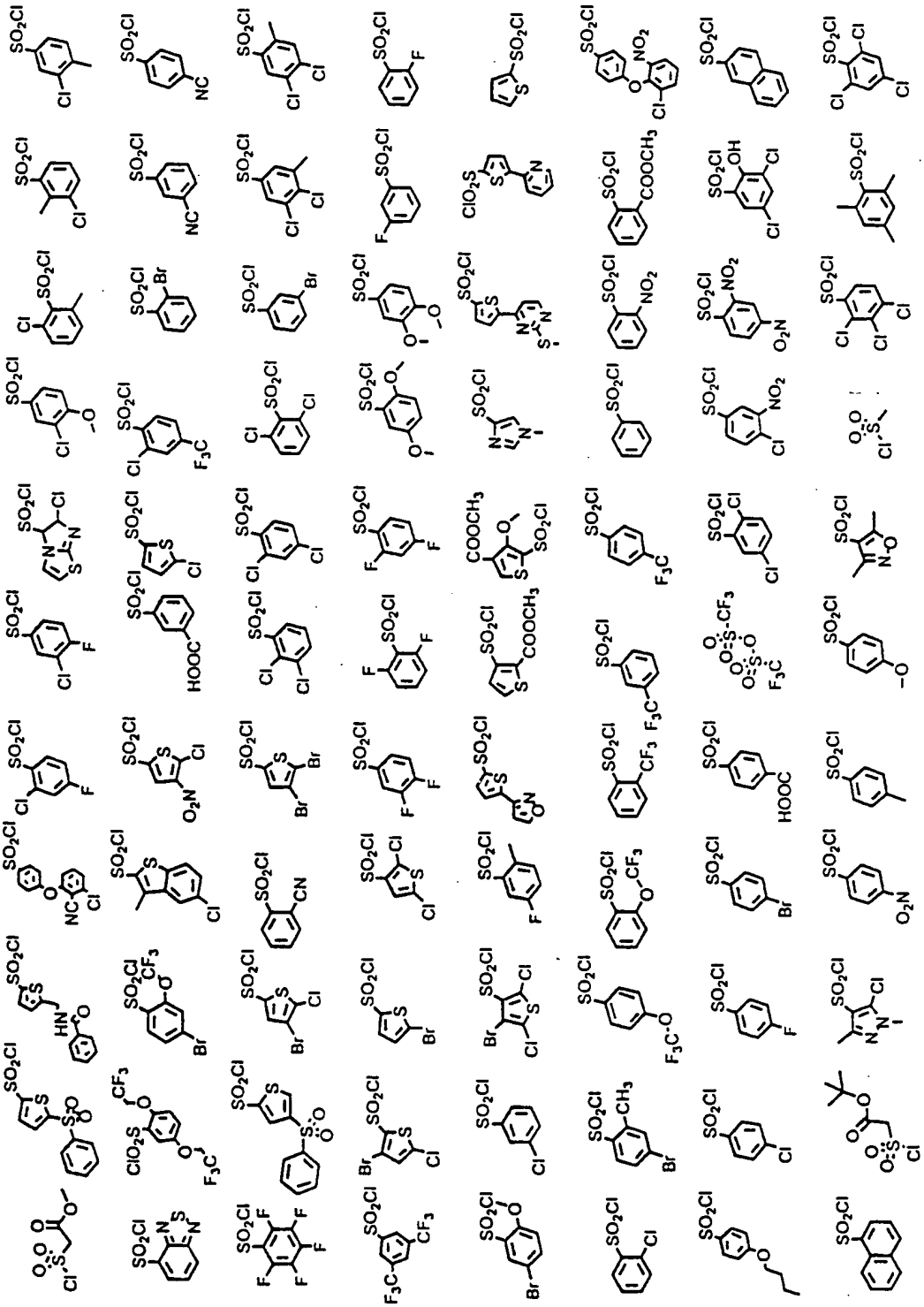


FIGURE 46

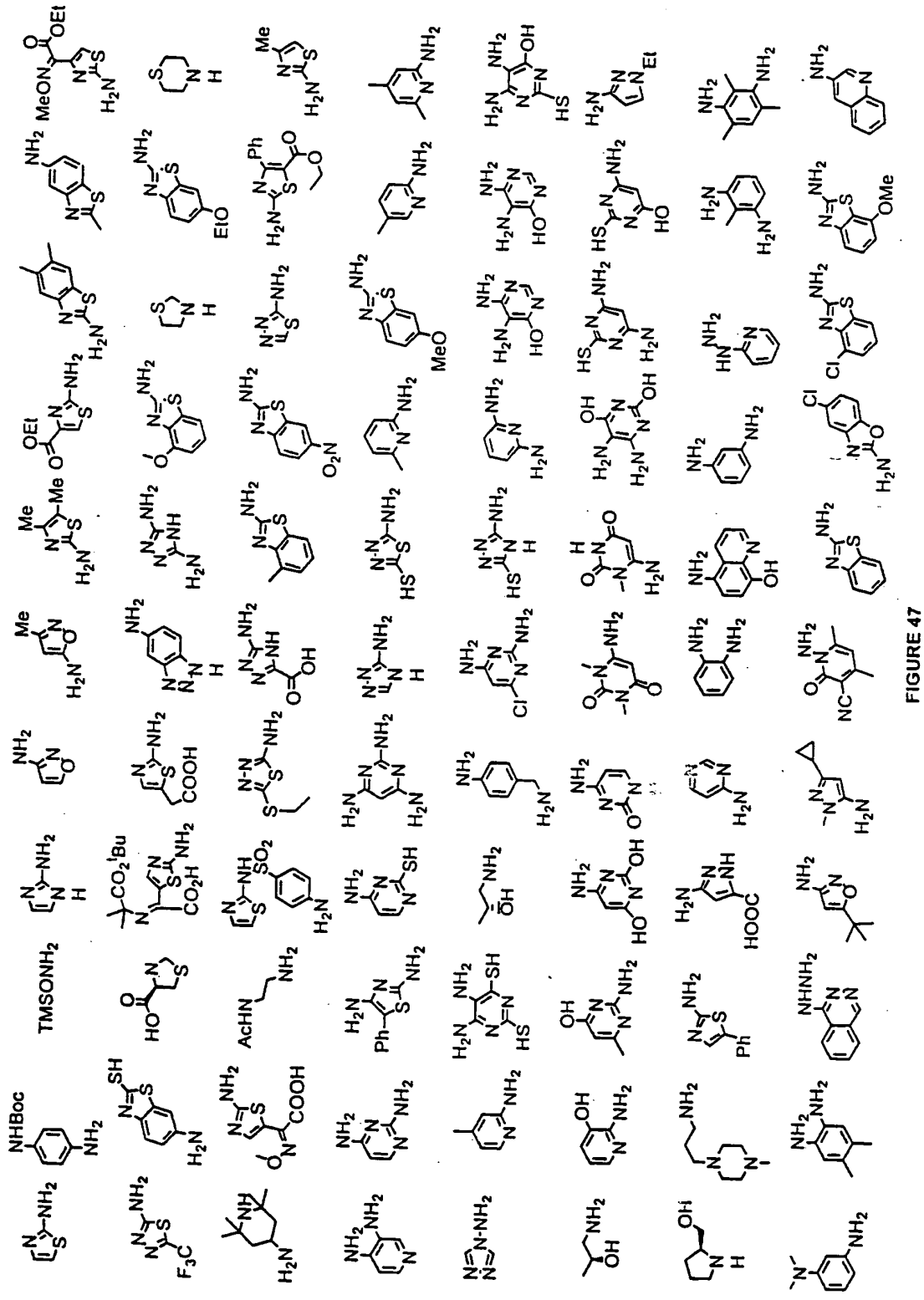
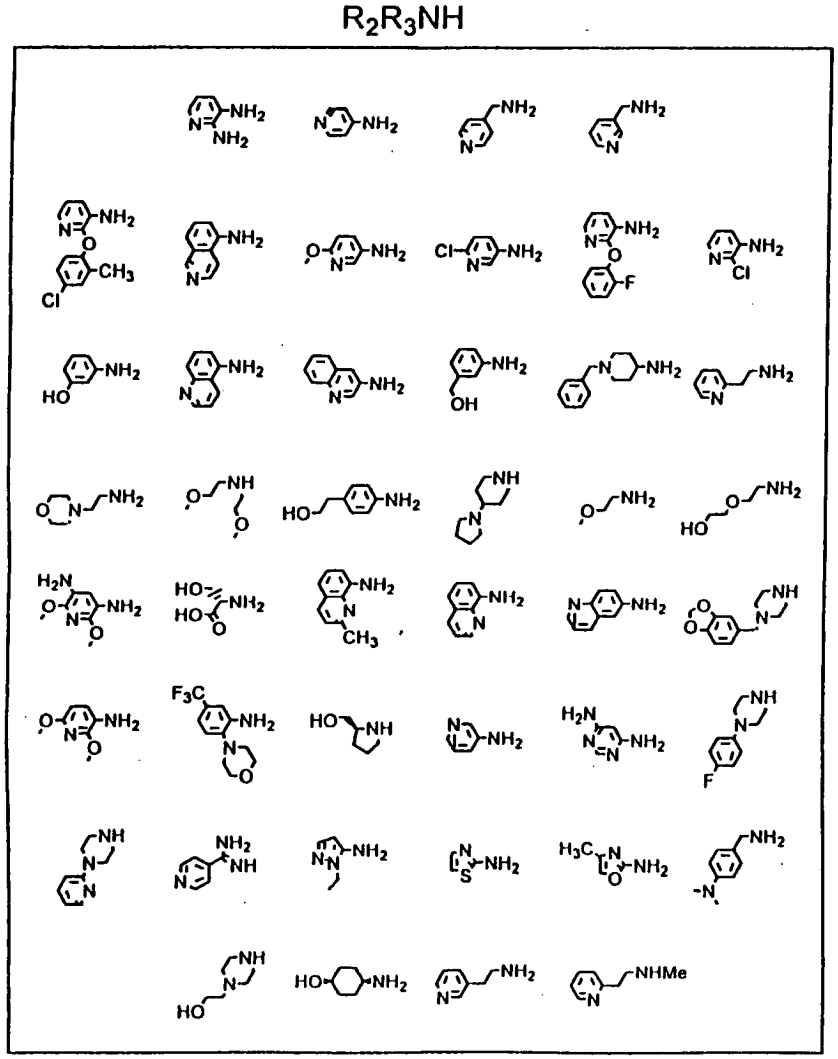
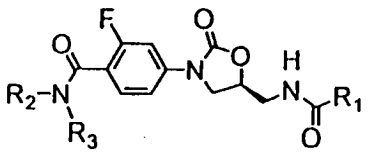


FIGURE 47





1k

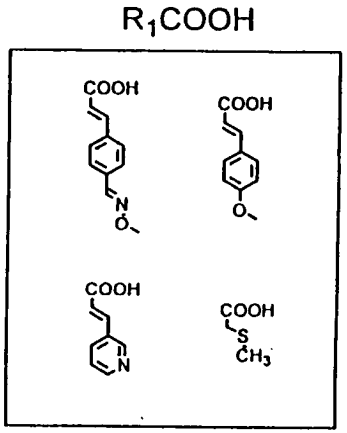


FIGURE 48

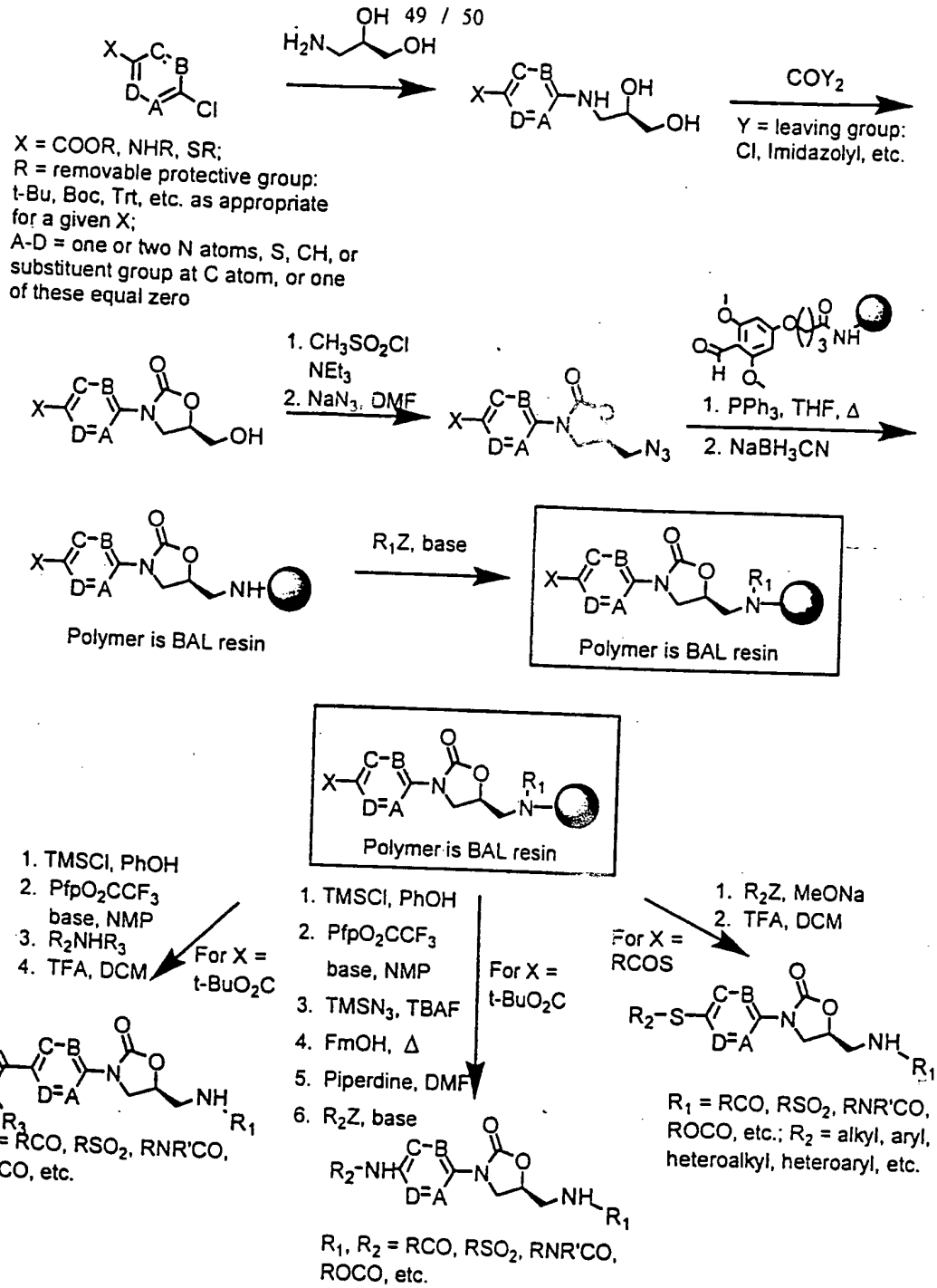
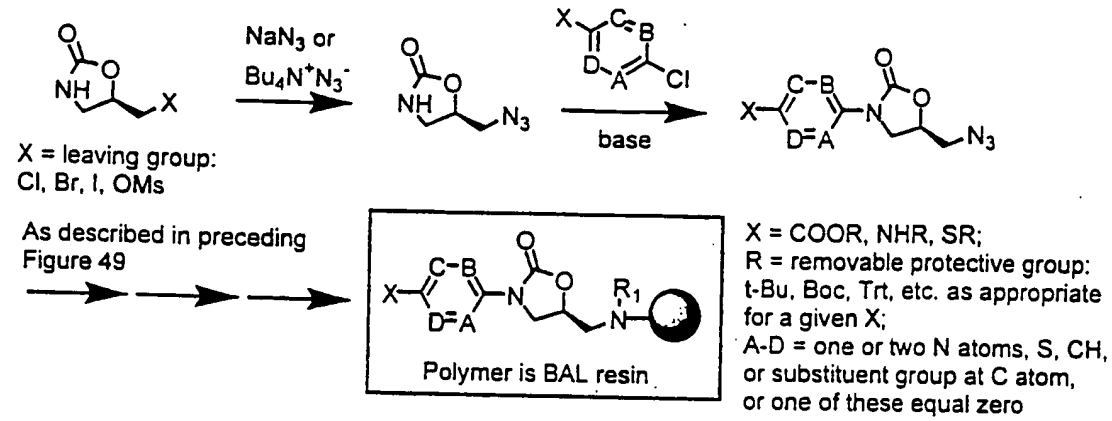

X = COOR, NHR, SR;
R = removable protective group: t-Bu, Boc, Trt, etc. as appropriate for a given X;
A-D = one or two N atoms, S, CH, or substituent group at C atom, or one of these equal zero
COY2
Y = leaving group: Cl, Imidazolyl, etc.
1. CH3SO2Cl
NEt3
2. NaN3, DMF
1. PPh3, THF, Δ
2. NaBH3CN
R1Z, base
Polymer is BAL resin
Polymer is BAL resin
Polymer is BAL resin
1. TMSCl, PhOH
2. PfpO2CCF3
base, NMP
3. R2NHR3
4. TFA, DCM
For X = t-BuO2C
R1 = RCO, RSO2, RNR'CO, ROCO, etc.
1. TMSCl, PhOH
2. PfpO2CCF3
base, NMP
3. TMSN3, TBAF
4. FmOH, Δ
5. Piperdine, DMF
6. R2Z, base
For X = t-BuO2C
R1, R2 = RCO, RSO2, RNR'CO, ROCO, etc.
1. R2Z, MeONa
2. TFA, DCM
For X = RCOS
R1 = RCO, RSO2, RNR'CO, ROCO, etc.; R2 = alkyl, aryl, heteroalkyl, heteroaryl, etc.

FIGURE 49

Synthesis from 5-(S)-azidomethyloxazolidinone



Synthesis from 5-(S)-(protected amino)methyloxazolidinone

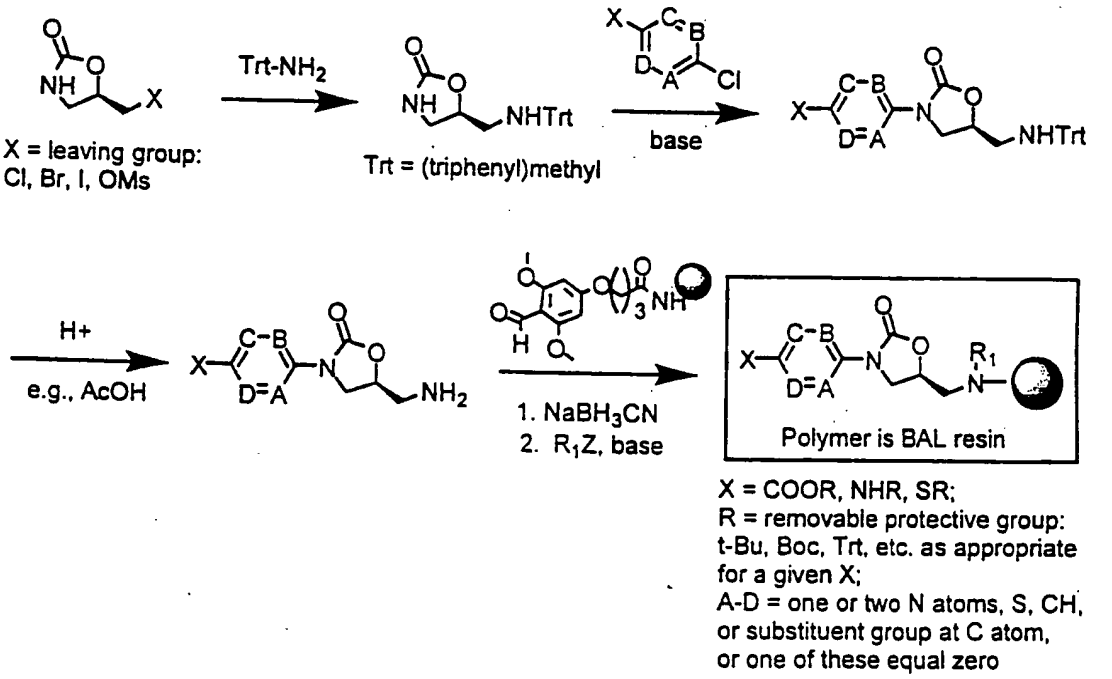


FIGURE 50

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D263/20 C07D413/12 C07D417/12 C07F9/653 C07D417/04
C07D413/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D C07B A61K C07F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 30981 A (PHARMACIA & UPJOHN CO) 28 August 1997 see claims ---	7-9, 13-43, 60-82,95
X	WO 97 21708 A (PHARMACIA & UPJOHN CO) 19 June 1997 see claims ---	7-9, 13-43, 60-82,95
X	WO 98 01446 A (ZENECA LTD) 15 January 1998 see claims --- -/---	7-9, 13-43, 60-82,95

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 April 1999	03/05/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Henry, J

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INTERNATIONAL SEARCH REPORT

Int. ional Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication,where appropnate, of the relevant passages	Relevant to claim No.
X	WO 98 01447 A (ZENECA LIMITED) 15 January 1998 see claims	7-9, 13-43, 60-82,95
X	WO 95 14684 A (UPJOHN CO) 1 June 1995 see claims	7-9, 13-43, 60-82,95
X	US 4 801 600 A (WANG CHIA-LIN J ET AL) 31 January 1989 see claims	7-9, 13-43, 60-82,95
X	WO 93 09103 A (UPJOHN CO) 13 May 1993 see claims	7-9, 13-43, 60-82,95
X	WO 93 23384 A (UPJOHN CO) 25 November 1993 see claims	7-9, 13-43, 60-82,95
X	WO 94 13649 A (UPJOHN CO) 23 June 1994 see claims	7-9, 13-43, 60-82,95
X	WO 95 07271 A (UPJOHN CO) 16 March 1995 see claims	7-9, 13-43, 60-82,95
X	WO 97 10223 A (PHARMACIA & UPJOHN CO) 20 March 1997 see claims	7-9, 13-43, 60-82,95
X	EP 0 127 902 A (DU PONT DE NEMOURS) 12 December 1984 see claims	7-9, 13-43, 60-82,95
X	EP 0 184 170 A (DU PONT DE NEMOURS) 11 June 1986 see claims	7-9, 13-43, 60-82,95
X	EP 0 312 000 A (DU PONT DE NEMOURS) 19 April 1989 see claims -/--	7-9, 13-43, 60-82,95

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INTERNATIONAL SEARCH REPORT

Int. ional Application No
PCT/US 99/01318

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 316 594 A (DU PONT DE NEMOURS) 24 May 1989 see claims	7-9, 13-43, 60-82,95
X	EP 0 352 781 A (DU PONT DE NEMOURS) 31 January 1990 see claims	7-9, 13-43, 60-82,95
X	EP 0 359 418 A (UPJOHN CO) 21 March 1990 see claims	7-9, 13-43, 60-82,95
X	EP 0 694 543 A (BAYER AG) 31 January 1996 see claims	7-9, 13-43, 60-82,95
X	EP 0 693 491 A (BAYER AG) 24 January 1996 see claims	7-9, 13-43, 60-82,95
X	DE 196 49 095 A (BAYER AG) 7 August 1997 see claims	7-9, 13-43, 60-82,95
X	DE 196 04 223 A (BAYER AG) 7 August 1997 see claims	7-9, 13-43, 60-82,95
A	WO 97 19039 A (NOVARTIS AG) 29 May 1997 see claims	1-6, 44-54
A	BALKENHOHL F ET AL: "COMBINATORIAL SYNTHESIS OF SMALL ORGANIC MOLECULES" ANGEWANDTE CHEMIE. INTERNATIONAL EDITION, vol. 35, no. 20, 1996, pages 2288-2237, XP002065423 see the whole document	1-6, 44-54
P,A	BUCHSTALLER H -P: "Solid Phase Synthesis of Oxazolidinones via a Novel Cyclisation/Cleavage Reaction" TETRAHEDRON, vol. 54, no. 14, 2 April 1998, page 3465-3470 XP004110492 see the whole document	1-6, 44-54

-/--

1

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INTERNATIONAL SEARCH REPORT

Int. ..ional Application No
PCT/US 99/01318

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
P,A	HOLTE P T ET AL: "Solid-Phase Synthesis of 3,5-Disubstituted 1,3-Oxazolidin-2-ones by an Activation/Cyclo-elimination Process" TETRAHEDRON LETTERS, vol. 39, no. 40, 1 October 1998, page 7407-7410 XP004133693 see the whole document -----	1-6, 44-54

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INTERNATIONAL SEARCH REPORT

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 95-100
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 95-100 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inta tional Application No
PCT/US 99/01318

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9730981 A	28-08-1997	AU 1954797 A	10-09-1997
		CA 2243706 A	28-08-1997
		EP 0883611 A	16-12-1998
WO 9721708 A	19-06-1997	AU 1407797 A	03-07-1997
		CA 2236677 A	19-06-1997
		EP 0868424 A	07-10-1998
WO 9801446 A	15-01-1998	AU 3352097 A	02-02-1998
WO 9801447 A	15-01-1998	AU 3352197 A	02-02-1998
WO 9514684 A	01-06-1995	AU 698699 B	05-11-1998
		AU 8010394 A	13-06-1995
		CA 2174107 A	01-06-1995
		CN 1135752 A	13-11-1996
		EP 0730591 A	11-09-1996
		JP 9505582 T	03-06-1997
		NZ 274966 A	26-01-1998
		US 5652238 A	29-07-1997
		ZA 9407885 A	09-04-1996
US 4801600 A	31-01-1989	AU 2350788 A	13-04-1989
		CA 1322001 A	07-09-1993
		DK 562888 A	10-04-1989
		EP 0311090 A	12-04-1989
		FI 884610 A	10-04-1989
		JP 1132569 A	25-05-1989
		PT 88713 B	31-12-1992
		SU 1616518 A	23-12-1990
		US 4921869 A	01-05-1990
		US 4985429 A	15-01-1991
		US 5032605 A	16-07-1991
		US 4965268 A	23-10-1990
		US 5036093 A	30-07-1991
		US 5036092 A	30-07-1991
		US 5039690 A	13-08-1991
WO 9309103 A	13-05-1993	AT 146783 T	15-01-1997
		AU 667198 B	14-03-1996
		AU 2689892 A	07-06-1993
		CA 2119556 A	13-05-1993
		DE 69216251 D	06-02-1997
		DE 69216251 T	15-05-1997
		DK 610265 T	09-06-1997
		EP 0610265 A	17-08-1994
		GR 3022340 T	30-04-1997
		JP 7500603 T	19-01-1995
		US 5565571 A	15-10-1996
		US 5801246 A	01-09-1998
		US 5654428 A	05-08-1997
		US 5756732 A	26-05-1998
		US 5654435 A	05-08-1997
WO 9323384 A	25-11-1993	AU 668733 B	16-05-1996
		AU 4287793 A	13-12-1993
		CA 2133079 A	25-11-1993
		CN 1079964 A	29-12-1993

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inte. ional Application No
PCT/US 99/01318

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9323384 A		CZ 9402505 A	16-08-1995
		EP 0640077 A	01-03-1995
		FI 945246 A	08-11-1994
		HU 72296 A	29-04-1996
		HU 9500659 A	28-11-1995
		IL 105555 A	15-07-1998
		JP 7506829 T	27-07-1995
		MX 9302665 A	01-11-1993
		NO 944237 A	04-01-1995
		PL 174909 B	30-10-1998
		PL 174850 B	30-09-1998
		SK 133794 A	07-06-1995
		US 5547950 A	20-08-1996
		US 5700799 A	23-12-1997
		ZA 9302855 A	24-10-1994
WO 9413649 A	23-06-1994	AT 161833 T	15-01-1998
		AU 670842 B	01-08-1996
		AU 5323994 A	04-07-1994
		CA 2147753 A	23-06-1994
		CZ 9501366 A	18-10-1995
		DE 69316240 D	12-02-1998
		DE 69316240 T	20-05-1998
		EP 0673370 A	27-09-1995
		ES 2111188 T	01-03-1998
		FI 952798 A	07-06-1995
		GR 3026228 T	29-05-1998
		HU 74099 A	28-11-1996
		JP 8504205 T	07-05-1996
		NO 952253 A	08-08-1995
		NZ 257031 A	26-07-1996
		PL 309283 A	02-10-1995
		SK 74695 A	11-10-1995
		US 5523403 A	04-06-1996
		CN 1092413 A	21-09-1994
		IL 107663 A	16-10-1996
		MX 9307705 A	30-06-1994
		ZA 9307791 A	20-05-1995
WO 9507271 A	16-03-1995	AU 687866 B	05-03-1998
		AU 7557094 A	27-03-1995
		CA 2168560 A	16-03-1995
		CN 1130379 A	04-09-1996
		EP 0717738 A	26-06-1996
		JP 9502436 T	11-03-1997
		NZ 271805 A	26-02-1998
		US 5880118 A	09-03-1999
		ZA 9405894 A	05-02-1996
WO 9710223 A	20-03-1997	AU 6964096 A	01-04-1997
EP 0127902 A	12-12-1984	AT 68490 T	15-11-1991
		AU 583250 B	27-04-1989
		AU 2909984 A	13-12-1984
		CA 1254213 A	16-05-1989
		CA 1275652 A	30-10-1990
		DE 3485162 A	21-11-1991
		DK 279584 A	08-12-1984

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inte .ional Application No
PCT/US 99/01318

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0127902 A		FI 842273 A,B,	08-12-1984
		GR 82361 A	13-12-1984
		IE 57619 B	10-02-1993
		JP 60008277 A	17-01-1985
		MX 169619 B	15-07-1993
		PT 78703 A	01-07-1984
		SU 1505442 A	30-08-1989
		SU 1426451 A	23-09-1988
		US 4705799 A	10-11-1987
EP 0184170 A	11-06-1986	AT 68491 T	15-11-1991
		AU 611627 B	20-06-1991
		AU 5081685 A	11-06-1987
		CA 1260948 A	26-09-1989
		DE 3584427 A	21-11-1991
		DK 561885 A	06-06-1986
		FI 854804 A,B,	06-06-1986
		GR 852919 A	07-04-1986
		IE 58325 B	08-09-1993
		JP 61134379 A	21-06-1986
		PT 81610 A,B	01-01-1986
		SU 1528317 A	07-12-1989
		US 4705799 A	10-11-1987
EP 0312000 A	19-04-1989	AT 73783 T	15-04-1992
		AU 2396288 A	20-04-1989
		CA 1320730 A	27-07-1993
		DE 3869310 A	23-04-1992
		DK 573988 A	17-04-1989
		FI 884755 A	17-04-1989
		GR 3004973 T	28-04-1993
		IE 60426 B	13-07-1994
		JP 1132570 A	25-05-1989
		NO 174551 B	14-02-1994
		PT 88765 B	31-12-1992
		SU 1616517 A	23-12-1990
		US 4942183 A	17-07-1990
EP 0316594 A	24-05-1989	AT 95176 T	15-10-1993
		AU 2404388 A	27-04-1989
		CA 1317594 A	11-05-1993
		DE 3884563 D	04-11-1993
		DE 3884563 T	17-02-1994
		DK 584188 A	22-04-1989
		ES 2059467 T	16-11-1994
		FI 884849 A	22-04-1989
		JP 1135777 A	29-05-1989
		PT 88811 B	30-04-1993
		SU 1801109 A	07-03-1993
		US 4977173 A	11-12-1990
EP 0352781 A	31-01-1990	US 4948801 A	14-08-1990
		AU 622465 B	09-04-1992
		AU 3911589 A	01-02-1990
		CA 1337526 A	07-11-1995
		DK 374389 A	30-01-1990
		FI 893618 A	30-01-1990
		JP 2124877 A	14-05-1990

INTERNATIONAL SEARCH REPORT

Information on patent family members

Intl Jonal Application No
PCT/US 99/01318

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0352781 A		PT 91315 A	08-02-1990
		US 5130316 A	14-07-1992
		US 5043443 A	27-08-1991
		US 5254577 A	19-10-1993
EP 0359418 A	21-03-1990	AT 112773 T	15-10-1994
		AU 617871 B	05-12-1991
		AU 4195789 A	02-04-1990
		CA 1335103 A	04-04-1995
		DE 68918792 D	17-11-1994
		DK 45591 A	13-03-1991
		EP 0434714 A	03-07-1991
		EP 0609905 A	10-08-1994
		HK 1002234 A	07-08-1998
		JP 2865211 B	08-03-1999
		JP 4500665 T	06-02-1992
		KR 138262 B	15-05-1998
		WO 9002744 A	22-03-1990
		US 5164510 A	17-11-1992
		US 5182403 A	26-01-1993
		US 5225565 A	06-07-1993
EP 0694543 A	31-01-1996	DE 4425612 A	04-04-1996
		AU 699940 B	17-12-1998
		AU 2498595 A	01-02-1996
		BG 99790 A	30-04-1996
		CA 2154025 A	21-01-1996
		CN 1119647 A	03-04-1996
		CZ 9501872 A	14-02-1996
		FI 953477 A	21-01-1996
		HR 950408 A	30-04-1997
		HU 75035 A	28-03-1997
		JP 8041056 A	13-02-1996
		NO 952865 A	22-01-1996
		NZ 272597 A	29-01-1997
		PL 309686 A	22-01-1996
		SG 33427 A	18-10-1996
		SK 91795 A	07-02-1996
		US 5627181 A	06-05-1997
		US 5843967 A	01-12-1998
		ZA 9506018 A	13-03-1996
EP 0693491 A	24-01-1996	DE 4425613 A	25-01-1996
		AU 695661 B	20-08-1998
		AU 2498895 A	01-02-1996
		BG 99791 A	30-04-1996
		CA 2154026 A	21-01-1996
		CN 1121919 A	08-05-1996
		CZ 9501873 A	14-02-1996
		FI 953476 A	21-01-1996
		HR 950391 A	30-06-1997
		HU 74003 A	28-10-1996
		JP 8053443 A	27-02-1996
		NO 952866 A	22-01-1996
		NZ 272596 A	24-03-1997
		PL 309685 A	22-01-1996
		SG 33428 A	18-10-1996
		SK 91695 A	07-02-1996

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter onal Application No
PCT/US 99/01318

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0693491 A		US 5698574 A	16-12-1997
		ZA 9506015 A	22-02-1996
DE 19649095 A	07-08-1997	AU 1251797 A	14-08-1997
		BG 101194 A	30-04-1998
		BR 9700903 A	18-08-1998
		CA 2196859 A	07-08-1997
		CZ 9700341 A	13-08-1997
		EP 0789026 A	13-08-1997
		HR 970049 A	30-04-1998
		HU 9700328 A	28-08-1998
		JP 10001480 A	06-01-1998
		NO 970512 A	07-08-1997
		NZ 314178 A	23-12-1998
		PL 318278 A	18-08-1997
		SK 15797 A	08-10-1997
DE 19604223 A	07-08-1997	AU 1251697 A	14-08-1997
		BR 9700885 A	27-10-1998
		CA 2196862 A	07-08-1997
		CN 1160051 A	24-09-1997
		CZ 9700340 A	13-08-1997
		EP 0789025 A	13-08-1997
		HR 970048 A	30-04-1998
		HU 9700358 A	28-07-1998
		JP 9316073 A	09-12-1997
		NO 970511 A	07-08-1997
		NZ 314179 A	23-12-1998
		PL 318277 A	18-08-1997
		SG 50791 A	20-07-1998
		SK 15897 A	08-10-1997
		US 5792765 A	11-08-1998
WO 9719039 A	29-05-1997	AU 7564296 A	11-06-1997